ACCIDENTAL HYPOTHERMIA

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"Man is a tropical animal and his physiological mechanism of homeostasis of body temperature is essentially adapted to tropical rather than cold climates" (Scholander et al. 1950).

ACCIDENTAL hypothermia is a well-known complication of exposure, myxœdema, and hypopituitarism, but may also be a very real hazard among the elderly population during the winter months. Although profound hypothermia is probably the cause of death in such familiar circumstances as exposure on the mountainside and on a raft at sea, it is only in recent years that attention has been effectively drawn, by Rees (1958) and by Emslie-Smith (1958) among others, to a form of hypothermia occurring mainly in debilitated elderly persons in no more hostile an environment than that of their own homes. Whereas hypothermia resulting from severe exposure may be regarded as "exogenous" and that associated with myxœdema as "endogenous", the condition with which we are concerned seems usually to involve both endogenous and exogenous factors in varying proportions. Although many of the elderly subjects in our study lay unprotected for long periods in cold rooms, there were several instances among our euthyroid patients where the fall of body-temperature could only be attributed to an innate impairment of the physiological responses of heat-conservation. Such cases may be more properly designated "spontaneous" hypothermia, but we have no wish to complicate the terminology. The elderly people affected

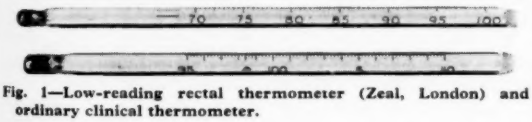

Fig. 1—Low-reading rectal thermometer (Zeal, London) and ordinary clinical thermometer.

usually live alone, in poor circumstances, and, by accident, illness, or mental confusion, are rendered unable to call for assistance. As their living quarters are almost always underheated, they become progressively colder, until a state of impaired consciousness supervenes. The degree of hypothermia will not be recognised unless a low-reading rectal thermometer (fig. 1) is used in all elderly patients where the clinical thermometer fails to register.

Hypothermia can be divided into three fairly distinct phases: (1) 98·4–90°F, in which the body reacts against increased chilling, the reaction being maximal at 95°F (Dill and Forbes 1941, Adolph 1951); (2) 90–75°F, where tissue metabolism throughout the body is depressed and the pulse, blood-pressure, and respiration decrease progressively with further fall of body-temperature; (3) below 75°F—here the temperature-regulating centre ceases to function and heat is lost from the body as from an inanimate object (Talbott et al. 1941).

It is not uncommon, during the winter months, to find temperatures of 94–97°F in elderly patients on admission to hospital, a normal temperature being regained within a day or two with no apparent ill effects. In this paper, however, we are concerned only with the second (and rarely the third) phase of hypothermia. The initial response to cold is represented by shivering, rise of blood-pressure, increase in pulse-rate, diuresis, and constriction of the skin capillaries; but below the range of 85–90°F shivering ceases and is succeeded by muscular rigidity, accompanied by a fine tremor which can be detected on the electrocardiogram. Consciousness is often impaired, and the skin is pale, cold, dry, and corpse-like; a variable degree of subcutaneous œdema is present. The pupils react poorly to light and the tendon reflexes may be delayed and sluggish. The respiratory and heart rates are depressed and the blood-pressure is low or unrecordable. The electrocardiogram may show the distinctive "J" or "Osborn" (Osborn 1953) waves. Death usually ensues at a body-temperature of around 77°F, but a remarkable case has been described of a young Negress who survived a rectal temperature of 64°F (Laufman 1951).

Material

All patients were admitted as emergency cases to wards of the medical or therapeutics professorial units, Dundee, or to the acute wards of the geriatric unit, Perth, during a period of three years between January, 1958, and January, 1961. Cases were included in the study only where the history and initial body-temperature met the requirements of accidental cold exposure with hypothermia. "Hypothermia" was arbitrarily selected as a rectal temperature of less than 90°F (32°C), in order to exclude temperature depressions of lesser degree occasionally associated with states of debility and illness (e.g., respiratory infections and congestive heart-failure) in elderly subjects. All the patients were elderly and many were living in isolation. In every instance the condition had developed whilst the patient was indoors; we have no information on the environmental temperature; and the duration of exposure to cold, whenever applicable, was assessed as accurately as possible.

The tabulated clinical (table I) and laboratory (table V) findings were those recorded at the time of admission. Associated diseases were noted, and an attempt was made to identify those precipitating factors that had led to prolonged exposure to cold and the development of hypothermia.

Clinical Findings

Age and Sex

With the exception of 1 patient, aged 56 years, all were elderly (see table I), with a preponderance of women. The cases were almost equally distributed among the three arbitrary types of body habitus (table II). This is rather surprising since it is known that as an insulator adipose tissue is twice as efficient as muscle (Bordier 1898).

Seasonal Distribution

Nearly all cases were admitted during the winter season and no cases were seen during the summer months. The distribution by months was as follows:

			No. of cases			
Jan.	*Feb.*	*March*	*April–Sept.*	*Oct.*	*Nov.*	*Dec.*
6	7	2	0	1	1	6

*Now consultant physician, Royal Infirmary, Aberdeen.

Circumstances and Duration of Exposure

Although the solitary circumstances of many patients made it difficult to obtain an accurate assessment of the duration of exposure, it was estimated that 15 had, for between six to forty-eight hours, been lying unattended in an unheated room, often on the floor. We were impressed, however, by the number of occasions where there was no evidence of such dire circumstances; these included 3 cases of myxœdema, 3 other patients who had been lying in bed in a reasonably warm room, an elderly lady sharing a home with her two sisters and confined to a chair because of extensively œdematous and ulcerated legs, and an old woman in good health who became stuck fast in a bottomless chair for almost forty-eight hours. All patients were discovered at home and indoors. 14 lived completely on their own, 4 were partially unattended (i.e., either all day or all night), and 5 were never left alone. Many were scantily clad—2 were almost naked—but 7 were adequately covered by clothes or blankets.

Condition on Admission

There was a rough correlation between depth of hypothermia and state of consciousness (table III). None of the 6 patients with temperatures below 80°F (26°C) was conscious, and only 1 of this group survived the episode of hypothermia; whereas, of the 16 patients with temperatures of 80°F (26°C) and above, 8 were fully conscious; the 6 survivors among this group included 4 who were conscious, 1 who was semiconscious, and 1 who was unconscious.

All patients were strikingly pale, and a distinctive "pliable" consistency of the subcutaneous tissue was sometimes noted on pinching the skin. The entire body-surface "radiated" a cadaveric frigidity, and not even relatively protected parts, such as the perineum and vulva, retained any warmth. Generalised muscular rigidity was present in most cases—at times so intense as to resemble rigor mortis; shivering was conspicuously rare, being noted in only 2 cases, with body-temperatures of 88°F (31°C) and 89°F (31°C). Peripheral œdema was present in over half the cases. Tendon-jerks were present in a majority of cases, and were actually exaggerated in several instances of severe hypothermia; they were described as "delayed" or "pendular" in 4 cases, and in 6 they could not be elicited. Fine muscular tremors, invisible to the naked eye, were often found as an artefact on the electrocardiogram (fig. 2). The pupils were more often constricted than dilated, reacting sluggishly, if at all, to light. Bradycardia was common, the heart-rate being less than 60 per minute in 16 of the 23 cases, and hypotension was noted in 12 cases where the systolic blood-pressure was less than 100 mm. Hg. Respirations tended to be shallow and slow, but on only 5 occasions was the rate below 12 per minute.

TABLE II—AGE, SEX, AND BODY HABITUS

Sex	Habitus			Totals	Age (yr.)
	Obese	Average	Thin		
M	1	3	2	6	68–80 (av. 75)
F	6	4	7	17	56–86 (av. 74)
Totals	7	7	9	23	56–86 (av. 75)

TABLE III—STATE OF CONSCIOUSNESS IN RELATION TO BODY-TEMPERATURE

State of consciousness	Temp. (°F)			
	70–74	75–79	80–84	85–89
Conscious	0	0	4	4
Semiconscious ..	0	2	1	2*
Unconscious ..	1	4	3	2†
Totals	1	6	8	8

* In these 2 cases (nos. 12 and 22), myxœdema and severe bronchopneumonia, respectively, were held to contribute to impairment of consciousness.

† Loss of consciousness was attributed in these 2 cases (nos. 16 and 21), to recent head injury and massive cerebral hæmorrhage, respectively.

Associated Conditions and Precipitating Factors

Associated physical and mental conditions, listed in table IV, were in many cases regarded as immediately

TABLE I—SUMMARY OF CLINICAL OBSERVATIONS

Case no.	Age (yr.)	Sex	Estimated duration of hypothermia (hours) *	Rectal temp. °F	Rectal temp. °C	State of consciousness ¶	B.P. (mm.Hg) ‡	Heart-rate/min.	Resp.-rate/min.	Associated conditions	J waves on E.C.G.	Course of hypothermia (°F)	Outcome §
1	84	F	12	87	30·5	C.	50/?	88	20	Senile, blind	–	87–99 in 24 hr.	R2
2	73	F	12	85	29·5	C.	70/?	44	7	Senile, semi-invalid	–	85–90 in 12 hr.	†<24hr.
3	68	F	24	82	27·5	C.	105/60	40	12	Chronic swelling and ulceration of legs	–	82–98 in 7 days	R1
4	75	F	12	73	23	U.C.	N.R.	12	4	Senile. Barbiturate poisoning	–	..	†<24 hr.
5	82	F	U.	78	25·5	S.C.	120/?	48	10	Mental deterioration	+	78–98 in 72 hr.	†<72 hr.
6	81	F	12	89	31·5	C.	N.R.	88	28	Cerebral thrombosis	..	89–99 in 24 hr.	R2
7	68	M	12	80	26·5	U.C.	N.R.	65	24	Chronic alcoholism. Recent coryza	+	80–90	†<24 hr.
8	63	F	24	82	27·5	C.	N.R.	N.R.	16	Bronchitis	..	..	†<24 hr.
9	73	M	24	83	28·5	S.C.	180/90	54	..	Bronchitis	+	83–97 in 4 days	R1
10	75	F	48	78	25·5	U.C.	N.R.	48	..	In good health. Wedged in bottomless chair	+	78–85	†<24 hr.
11	75	F	12	80	26·5	U.C.	180/85	40	20	Myxœdema	+	..	†<24 hr.
12	83	F	U.	85	29·5	S.C.	140/60	104	30	Myxœdema. Mental deterioration	+	..	†<24 hr.
13	63	F	U	88	31	C.	180/80	40	20	Myxœdema. Falling at home—"off legs"	..	88–99 in 6 days	R1
14	72	F	48	76	24·5	U.C.	N.R.	30	12	Myxœdema	+	76–86	†<48 hr.
15	56	F	12	82	27·5	C.	90/?	32	8	Myxœdema	–	82–85	†<24 hr.
16	82	F	24	86	30	U.C.	120/?	44	..	Lt. leg amputee 25 yr. Recent head injury	+	..	†<24 hr.
17	75	M	24	77	25	U.C.	N.R.	40	30	Chronic pyelonephritis and renal calculi. Recent head injury	+	77–82	†<24 hr.
18	81	F	12	80	26·5	U.C.	120/80	60	16	Mental depression. Barbiturate poisoning	+	80–101 in 24 hr.	R3
19	86	F	U.	79	26	U.C.	50/30	28	14	Mental confusion. Varicose ulcers of legs	..	..	†<24 hr.
20	80	M	12	77	25	S.C.	115/50	40	10	Mental confusion. Diabetes mellitus	+	77–98 in 24 hr.	R4
21	75	M	12	88	31	U.C.	100/?	80	28	Massive cerebral hæmorrhage	–	88–98	†<24 hr.
22	80	M	U.	89	31·5	S.C.	40/?	60	20	Cerebral arteriosclerosis. Bronchopneumonia	–	89–97	†<48 hr.
23	82	F	U.	82	27·5	C.	105/60	78	22	Bronchopneumonia	–	82–97	†<24 hr.

Vital indices (i.e., rectal temperature, blood-pressure, heart-rate, and respiration-rate) are those recorded at initial examination.
* U. = unknown. ¶ C. = conscious; S.C. = semiconscious; U.C. = unconscious. ‡ N.R. = not recordable. § R1 = complete recovery; R2 = recovered but died later from C.V.A.; R3 = recovered but died later from C.V.A. and bronchopneumonia; R4 = recovered but died later from bronchopneumonia. † = died.

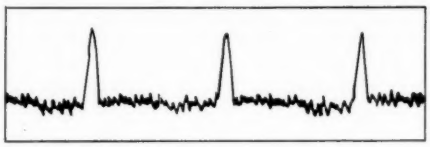

Fig. 2—Electrocardiogram showing characteristic distortion caused by fine muscular tremors.

responsible for the long exposure to cold and resultant hypothermia or for the impairment of the physiological responses of heat conservation in those cases with no history of severe exposure. Senile mental impairment predisposed to the development of hypothermia in 8 cases, and there were 5 cases of myxœdema hypothermia. In addition to 2 cases of bronchopneumonia, acute infection of the lower respiratory tract was regarded as a precipitating factor on 3 occasions.

The Electrocardiogram

Direct electrocardiographic recordings were made in 19 cases within an hour or two of admission. Lengthening of the PR and QRS intervals was commonly seen, and varying degrees of conduction defect occurred in almost half the cases. The distinctive J deflection (or Osborn wave), occurring at the junction of the QRS complex and ST segment, was found on 11 occasions, seldom of high amplitude and almost entirely confined to the left chest leads (fig. 3). A common artefact, already mentioned, was attributed to fine muscular tremors.

TABLE IV—PRINCIPAL CONDITIONS ASSOCIATED WITH OR PREDISPOSING TO ACCIDENTAL HYPOTHERMIA

Condition	No. of cases
Mental impairment and senility	8
Myxœdema	5
Recent fall and head injury	2
Mechanical restriction of activities	2
Barbiturate intoxication	2
Cerebrovascular accident	2
Bronchopneumonia	2

Laboratory Investigations

Hæmatology

The hæmoglobin varied from 28 to 125% (5·3 to 18·5 g. per 100 ml.); readings of 105% (15·6 g.) and over were recorded in 8 cases, falling to lower levels during the subsequent twenty-four hours. The hæmatocrit ranged from 34 to 62. The white-blood-cell count varied from 750 to 12,600 per c.mm., with normal differential counts. Very limited investigations of the blood-coagulation mechanisms showed no consistent deviations from the normal, but it would probably have been more meaningful to perform such tests at the temperature of the hypothermic patient.

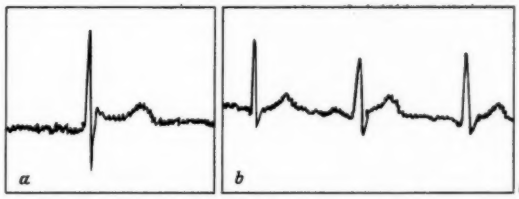

Fig. 3—Electrocardiogram in case 17 showing: *a*, typical J deflection; and *b*, tracing from same patient six months previously.

Biochemistry (table V)

Plasma-bicarbonate, estimated in 14 cases, varied from 10·3 to 29·6 mEq. per litre, with distinctly low values in 6. The blood-sugar varied from 50 to 316 mg. per 100 ml., the exceptionally high value being obtained in a diabetic subject. The blood-urea was moderately raised in most cases, varying from 20 to 220 mg. per 100 ml., and later showing a progressive downward trend. Serum-cholesterol was determined in 14 cases; the values were normal in all except in 2 patients with myxœdema; in the other 3 cases of myxœdema the values fell within the normal range—a finding noted in 19% of a large series reported by Wayne (1960). Patients with myxœdema and normal blood-cholesterol were hard to differentiate clinically

TABLE V—BIOCHEMICAL INVESTIGATIONS

Case no.	Plasma-bicarb. (m.Eq. per l.)	Blood-sugar (mg. per 100 ml.)	Serum-cholesterol (mg. per 100 ml.)	Blood-urea (mg. per 100 ml.)	Serum-creatinine (mg. per 100 ml.)	Serum Na. (mEq. per l.)	Serum-Cl. (mEq. per l.)	Serum-K. (mEq. per l.)	Serum-amylase (units)	Serum-transaminase (G.O.T. units)	Serum-alk.-phosphatase (K.A. units per 100 ml.)	Serum-proteins (g. per 100 ml.)*	Serum-bilirubin (mg. per 100 ml.)	Thymol turbidity (units)	Serum-calcium (mg. per 100 ml.)	Serum-phosphorus (mg. per 100 ml.)	Reaction of urine
1	24·5	170	180	100	1·5	139	105	5·3	145(S.)	..	6·0	5·2 (2·8, 2·4)	0·4	2·0	..	..	Acid
2	..	145	258	95	1·4	139	110	6·2	156(S.)	..	..	..	..	..	..	..	..
3	22·0	56	143	20	0·9	140	107	5·0	160(S.)	..	4·0	6·3 (2·2, 4·1)	0·6	3·0	9·5	..	Acid
4	29·6	188	100	85	2·4	145	99	4·7	535(S.)	..	9·0	5·0 (3·2, 1·8)	0·2	1·0	10·0	..	..
5	26·0	149	241	48	1·1	135	101	5·4	1066(S.)	..	7·5	5·2 (3·4, 1·8)	1·2	0·5	..	..	Acid
6	17·0	126	164	55	1·7	147	107	3·7	320(S.)	..	4·8	4·9 (3·0, 1·9)	0·8	0·5	..	..	Acid
7	10·3	283	..	220	..	145	105	7·3	2540(S.)	119	..	7·6 (5·1, 2·5)	..	..	..	..	..
8	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
9	10·9	149	159	77	1·3	148	105	4·7	20(S.-C.)	23	..	5·5 (3·7, 1·8)	..	..	..	..	Acid
10	12·2	116	108	84	..	152	108	4·6	55(S.-C.)	..	..	..	..	..	..	..	Acid
11	..	..	550	..	..	..	..	..	..	..	..	..	..	..	..	..	..
12	26·1	147	195	37	..	140	100	3·2	4000(S.)	..	22·5	6·0	0·4	..	10·0	..	..
13	27·4	79	235	42	..	147	105	4·3	400(S.)	..	..	7·3 (3·9, 3·4)	..	..	10·0	..	Acid
14	..	50	185	45	..	..	..	..	..	..	..	..	..	..	..	..	..
15	25·0	130	356	35	..	134	96	3·5	[illegible] S.)	112	13·0	6·2 (3·7, 2·5)	0·3	1·0	10·0	1·9	Acid
16	..	..	..	45	..	..	..	..	..	..	..	..	..	..	..	..	..
17	10·9	..	..	..	..	..	..	6·	[illegible] S.)	..	..	..	..	..	..	..	..
18	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
19	..	..	..	49	..	142	96	4·5	..	..	..	5·5 (3·4, 2·1)	..	..	..	..	Acid
20	29·0	316	..	..	..	..	..	..	..	..	..	..	..	..	..	..	Alk.
21	25·7	70	165	35	3·0	134	104	5·0	400(S.)	37	7·1	6·7 (4·0, 2·7)	..	..	10·3	3·6	Acid
22	..	..	..	68	..	146	103	4·6	43(S.-C.)	40	..	..	..	..	..	..	..
23	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..

* Serum-albumin and serum-globulin shown in parentheses.

Normal values for the serum-enzyme determinations by the methods employed are as follows:
Amylase: 80–180 Somogyi (S.) units, 6–30 Street-Close (S.C.) units.
Glutamic oxaloacetic transaminase (G.O.T.), 12–36, Sigma-Frankel units at 25°C.
Alkaline phosphatase 3–12 King-Armstrong (K.A.) units.

Fig. 4—Case 3: (*a*) soon after admission, showing bloated, "myxœdematous" features; (*b*) two weeks after recovery from hypothermia. The patient was not myxœdematous and received no thyroid therapy.

from euthyroid patients, of whom at least 1 looked puffy and grossly "myxœdematous" during the period of hypothermia but later reverted to a normal appearance without thyroid therapy (fig. 4). Serum-electrolyte determinations, in 16 patients, showed scarcely any deviation from the normal pattern. The conventional tests of liver function (serum-proteins, serum-alkaline-phosphatase, serum-bilirubin, and thymol turbidity) were performed in 12 cases, and the only significant deviations from the normal were in the serum-proteins. Total protein was less than 6 g. per 100 ml. in 6 cases and albumin less than 4 g. per 100 ml. in 9 cases, the albumin-globulin ratio being reversed on only one occasion.

Among the most striking biochemical findings was the high prevalence of raised serum-amylase values. Of 15 cases where serum-amylase was estimated, it was elevated in 11. Of these 11, 5 were found at necropsy to have evidence of pancreatic necrosis, 1 had non-suppurative parotitis, and 1 had no necropsy; in the remaining 4 cases the raised serum-amylase levels could not be explained, even at necropsy. In 4 of the 5 patients in whom serum-transaminase estimations were made during hypothermia, the results were above normal. The patient with the highest level (119 units) did in fact have micro-infarcts of the myocardium, although the naked-eye appearance of the heart at necropsy in this case, as in the others, was normal.

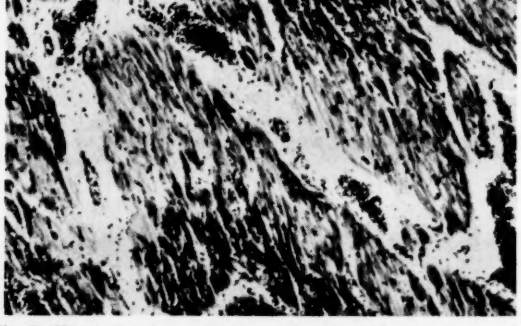

Fig. 5—Heart, showing congestion and areas of focal necrosis with polymorphonuclear infiltration (hæmatoxylin and eosin. ×80).

The Outcome

As can be seen in table I, 7 patients recovered from the episode of hypothermia. Of these, 3 recovered completely and were eventually discharged from hospital healthy and active. The complete absence of residual signs of cerebral dysfunction was particularly noteworthy in one patient who remained hypothermic and unconscious for seven days. 4 other patients became conscious and normothermic within twenty-four hours of admission, but succumbed later to an intercurrent illness. The time taken for the body-temperature to return to the normal level varied from eighteen hours to seven days. The remainder—16 cases—died in hypothermia, 13 within twenty-four hours of admission.

Pathology

Postmortem examinations were made in 13 of the cases in which the patient died during the episode of hypothermia. Interpretation of the findings was rendered difficult by the advanced age of the patients, the non-specific character of many of the changes, and the presence of concomitant disease. The immediate cause of death in all cases was considered to be central and peripheral circulatory failure. Pre-existing cardiac hypertrophy was present in 5 cases and significant coronary sclerosis in 2. A macroscopically visible infarct, associated with coronary thrombosis, was found in 1. 3 also showed small areas of infarction (micro-infarcts) in the ventricles, associated in 1 with moderate coronary stenosis (fig. 5). The heart-muscle showed fatty change in every instance. This was taken to represent the fatty metamorphosis that occurs in hypothermia (Knocker 1955) since it was found also in liver and renal tubules, and in increased amount in the zona reticularis of the adrenals. Apart from this, the lesions were similar to those described in the circulatory insufficiency of the shock phase of the stress reaction (Selye 1950) or in hypoxia (Knocker 1955).

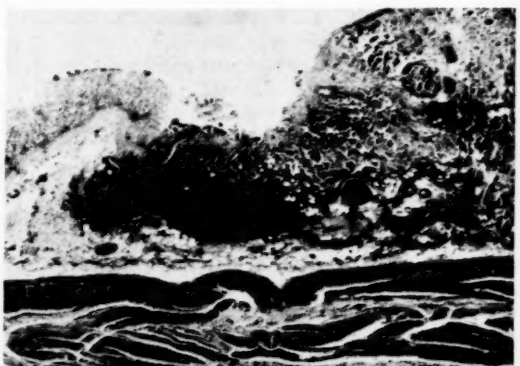

Fig. 6—Stomach, showing a hæmorrhagic erosion (hæmatoxylin and eosin. ×10).

Specific changes, compatible with either shock or hypoxia, were found in the gastrointestinal tract, pancreas, parotids, and brain (Moon and Kenny 1932, Rukinstat 1932, Sano and Smith 1940, Selye 1950, Maguire 1955, Kayser 1957). Acute gastric erosions were found in 3 cases and mucosal hæmorrhages in 3 others (fig. 6). Acute hæmorrhagic pancreatitis was present in 2 cases and focal pancreatic and fat necrosis in 3 others (fig. 7). In one case of recurring episodes of hypothermia (not included in the

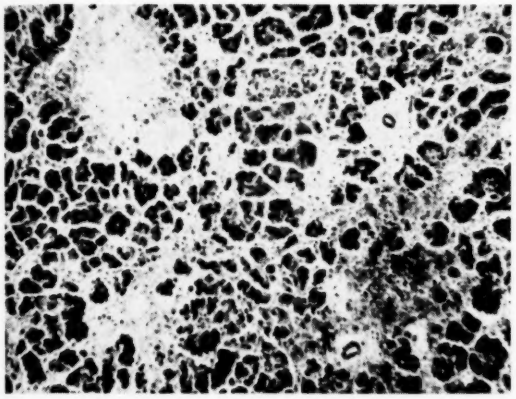

Fig. 7—Pancreas, showing focal areas of hæmorrhage and necrosis (hæmatoxylin and eosin. ×80).

series) both chronic and acute pancreatitis were found. There was 1 example of necrotising parotitis, where the parotids were specifically examined because of high serum-amylase levels during life and absence of naked-eye changes in the pancreas.

The brain was examined microscopically on 5 occasions. Perivascular hæmorrhages, in the region of the third ventricle, associated with chromatolysis of ganglion cells, were found in 2 (fig. 8), while another showed petechiæ of the leptomeninges.

Finally, multiple visceral infarcts were found in several cases, as follows: small bowel (1), lung (1), spleen (2), kidney (1), brain (3), and (already mentioned) heart (3). Histological examination indicated that they were caused by stagnation of blood with tight packing of red blood-cells (sludging of blood) in adjacent arterioles and capillaries, probably occurring during the period of circulatory collapse. Thrombus formation in smaller veins was an added feature in several cases.

It seems unnecessary to separate the lesions of hypoxia (Knocker 1955) from those caused by shock (Selye 1950), since the combination of circulatory collapse, hæmoconcentration with sludging of blood in the capillaries, and depressed cellular metabolism found in uncontrolled hypothermia renders the tissues less able to use the oxygen which is present at normal tension. This reduction in oxygen requirement by the tissues forms the basis of the use of controlled hypothermia to combat shock (Maguire 1955, Kenny 1956, Kayser 1957), but there initial shivering and circulatory collapse are not allowed to occur.

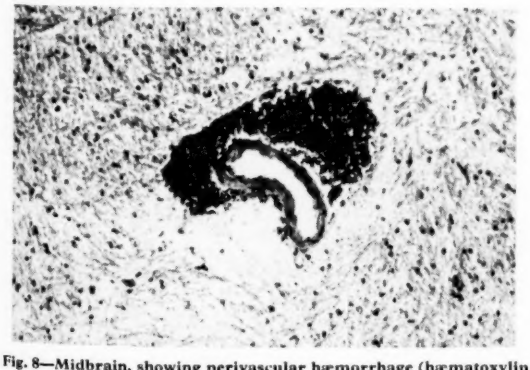

Fig. 8—Midbrain, showing perivascular hæmorrhage (hæmatoxylin and eosin. ×100).

Treatment

Since most of the patients were in a critical condition and no specific therapy was available, our main concern was that treatment should be harmless and as rational as our understanding of the altered physiology of hypothermia would permit.

Active Rewarming

To warm or not to warm is probably the most fundamental issue in the management of these patients, and rapid restoration of the body-temperature to a normal level might be regarded as a natural objective. There are several ways of attempting this, such as immersion in a hot bath, the use of a heat cradle or electric blankets, and warm intragastric or intravenous infusions. Attempts at active rewarming were made in 6 of our earlier cases, all of whom promptly died.

The main danger of relatively rapid rewarming seems to lie in the abolition of the intense peripheral vasoconstriction which compensates for reduced blood-volume in the chilled state. Rapid release of vasoconstrictor tone would result in circulatory failure, as well as "after-drop" in the temperature of the body "core" caused by redistribution of blood from the cold skin to warmer central organs. It has also been shown that warming the skin inhibits endogenous heat-production (Adolph 1950). Whether or not those earlier deaths were accelerated by active rewarming, it was decided thereafter to abandon this form of treatment. The patient was merely insulated against further cooling by a blanket and spontaneous rewarming was allowed to take place in a warm room, thereby allowing the physiological changes to reverse slowly and preventing the circulatory dangers of too rapid rewarming. It may be significant that, out of 17 patients so treated, 7 survived the episode of hypothermia. It has occurred to us that, since the heart is so particularly vulnerable at low temperatures, attempts might safely be made to apply warmth to the heart itself without actively rewarming the rest of the body. This might be accomplished by the heat provided by hot-water bottles, electric heat pads, or infra-red radiation applied to the precordium, or directly by means of diathermy. But, particularly where diathermy is used, most patients suffering from accidental hypothermia will not be sufficiently conscious to indicate a tolerable temperature on the chest wall, and burning might result.

Antibiotics

Antibiotics, mainly in the form of penicillin, either alone or combined with streptomycin, were given to all patients to guard against, or to treat, lower-respiratory-tract infection. It was considered that such patients might be prone to infection because of the common findings of pulmonary œdema and depressed respiration.

Oxygen

Oxygen was not used in treatment, despite the tendency to respiratory depression, since experimental work has shown that the oxygen tension of the blood in hypothermia is high, so that the giving of oxygen may actually precipitate carbon-dioxide narcosis (Severinghaus 1956b).

Parenteral Fluids

These were given to almost all of the patients. In many patients consciousness was impaired, while the remainder were too weak to maintain an adequate fluid intake by mouth. The main clinical indications for parenteral fluid therapy are severe hypotension and/or hæmoconcentration. The hypotension can be corrected with plasma or plasma-

substitute and the hæmoconcentration with 5% dextrose solution. There does not seem to be a specific need for saline, which may tend to increase the danger of pulmonary œdema. Glucose was preferred, as a nutriment and also to counteract a tendency for the blood-sugar to fall as the body temperature rose from hypothermic levels.

The immediate purpose, then, of fluid administration is to augment the blood-volume and to correct hæmoconcentration, since in hypothermia there occurs a shift of fluid from the vascular space to the interstitial tissues, leading to reduced blood-volume, hæmoconcentration, and increased blood viscosity. (Such intrinsic shifts in the distribution of body-water complicate the interpretation of the results of serum-electrolyte determinations.) On the other hand, diminished urinary excretion, particularly in the presence of hypotension, together with the common tendency to pulmonary and peripheral œdema, must indicate caution in the use of parenteral fluids. In only 1 of our cases, however, was excessive fluid administration held responsible for severe pulmonary œdema.

Corticosteroid Hormones

Hydrocortisone was given, parenterally, to many of the severely hypothermic or hypotensive patients—mainly as a general supportive measure. We feel in retrospect that there may be more adequate reasons for such therapy. Thus both Bernhard (1956) and Hume (1956) have shown that hypothermia depresses the output of corticotrophin and of adrenal cortical hormones under conditions of stress. Also, the sensitivity of the dog's adrenal cortex to exogenous corticotrophin is much depressed by hypothermia (Hume et al. 1956). Apparently, hypothermia does not in itself constitute a stress situation for the adrenal glands, although a cold environment in the absence of hypothermia of the tissues does do so (Selye 1950). The effect of cold in depressing adrenal cortical activity seems to be a direct one on the adrenals, as shown by the effect of local application of cold to the adrenals in an otherwise normothermic animal (Hume et al. 1956). Possibly the circulatory collapse which so regularly follows the rapid rewarming of hypothermic patients is due partly to the development of acute adrenal insufficiency, the body's requirement for the cortical hormones exceeding the power of the adrenal glands to supply them (Severinghaus 1956a). Many of the necropsy findings in our cases, such as acute gastric ulceration, acute pancreatitis, and visceral micro-infarcts, are suggestive of the changes found in the severe shock phase of stress, and it has been shown that such changes occur particularly rapidly in the absence of the pituitary and adrenal glands (Selye 1950). Hypothermia with rectal temperature under 90°F is associated with a progressive decrease in the secretory activity of the pituitary and adrenal cortices until at 78°F, in dogs, a state resembling functional hypophysectomy is produced (Egdahl and Richards 1956). It seems likely, then, that the hæmorrhagic lesions in the gut, brain, and pancreas, as well as the gastric erosions and focal pancreatic necrosis, found in our patients occurred during the phase of hypothermia with its attendant deficiency of pituitary and adrenal cortical activity. Such an interpretation of our findings provides a logical basis for administration of hydrocortisone as a means of preventing or minimising such lesions during hypothermia.

Vasoconstrictors

Vasoconstrictor drugs such as noradrenaline or mephentermine sulphate were used in most of the hypotensive cases, in an attempt to raise the blood-pressure and to prevent renal cortical necrosis and irreversible damage to the brain. No clear benefit from the use of these agents was noted in our limited and uncontrolled series, but there are several theoretical reasons for their use. Thus, Hume et al. (1956) found distinct and progressive decrease in the secretion of adrenaline and noradrenaline in the adrenal venous blood of hypothermic dogs, while Reissmann and Kapoor (1956) noted a decreased response of the hypothermic dog's heart to the cardio-accelerator effect of adrenaline. Perhaps the strongest reason for using catecholamines is to prevent the cutaneous vasodilatation that results from active rewarming of hypothermic patients. Such peripheral vasodilatation is clearly undesirable because of its hypotensive effect and the fact that relatively warm blood previously circulating mainly in the " core " of the patient is chilled by passage through the colder periphery with subsequent cooling of the " core ", and in particular the heart. Thus continuous slow intravenous infusions of noradrenaline might improve the results of active rewarming in the treatment of spontaneous or accidental hypothermia. Further, work on rats has shown that adrenaline and noradrenaline are particularly potent in raising the body-temperature under hypothermic conditions, and it has been suggested that they are mainly responsible for generation of heat after shivering has ceased (Depocas 1961). Infusions of noradrenaline might therefore be expected to stimulate the natural warming process in recovery from hypothermia. Finally, as Fruehan (1960) has emphasised, a careful search must be made for predisposing factors which may have been responsible for the exposure to cold and fall in body-temperature and also for the presence of associated diseases, which are commonly found in elderly patients.

Summary

A series of 23 cases of accidental hypothermia is described. All were elderly patients in whom hypothermia (rectal temperature less than 90°F [32°C]) had developed indoors. In 6 patients—including 3 with myxœdema—hypothermia had developed " spontaneously ", without excessive exposure to cold.

Predisposing or precipitating factors included mental impairment and senility (8), myxœdema (5), and bronchopulmonary infection (5).

Depth of hypothermia, state of consciousness, and survival were fairly closely correlated. None of the 6 patients with temperatures below 80°F (26°C) was conscious, and only 1 of these survived.

Characteristic J waves were seen in the electrocardiogram in 11 out of 19 patients. Laboratory investigations gave some evidence of hæmoconcentration and acidosis. Of 15 cases in which serum-amylase was estimated increased values were found in 11; and in 5 of those evidence of pancreatic necrosis was found at necropsy.

7 patients survived the episode of hypothermia; most of the remainder died within twenty-four hours of admission. Postmortem examinations were made in 13 cases. Significant findings included visceral micro-infarcts, gastric erosions, and pancreatic necrosis.

Elderly patients with accidental hypothermia should not be actively rewarmed.

We should like to thank Prof. I. G. W. Hill, Prof. R. B. Hunter, Dr. R. Semple, Dr. W. Walker, and Dr. I. D. Easton for permission to study cases under their care. We are also indebted to Dr. G. H. Smith for help and advice on pathology, to Dr. Mary Shaw for clinical assistance, and to Dr. F. L. Mitchell (Dundee), Mr. F. J. M. Robertson (Perth), and Mr. J. Comrie (Perth) for the biochemical estimations. The photographs were kindly supplied by Mr. Adam

Tilp, department of clinical photography, Bridge of Earn Hospital, and by Mr. J. Corkhill, department of pathology, Queen's College, Dundee.

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PANCREATITIS AND ACCIDENTAL HYPOTHERMIA

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IN 1940 Sano and Smith, whilst investigating the the necropsy findings in 50 patients who had been treated with hypothermia for various malignant disorders, noted pancreatitis, focal and diffuse, in 5 of them. Emslie-Smith (1958) has recorded similar necropsy findings in a patient with myxœdema who died while hypothermic. Duguid et al. (1961) report changes in the pancreas (focal necrosis or acute and chronic pancreatitis) in 5 of 23 patients with accidental hypothermia.

We have recently studied 2 patients with accidental hypothermia and biochemical evidence of pancreatic damage; and in 1 of them the pancreatitis had a histologically unusual form. Since the prognosis of spontaneous hypothermia is poor even when the patient's initial progress and rise of temperature are satisfactory, the possibility of pancreatic lesions deserves attention.

The Cases

FIRST CASE

A woman now aged 86 was admitted to hospital in 1960. When she was first seen, in 1941, a barium-meal examination showed a duodenal ulcer, and in 1956 a Billroth I partial gastrectomy was performed. In 1959 she complained of a sore mouth and tongue and she was found to be anæmic, with a megaloblastic bone-marrow. The serum-B_{12} level was normal (310 μμg. per ml.) and she responded well to iron and folic acid by mouth. Her diet had been poor, and her anæmia was attributed to inadequate intake of folic acid. She improved greatly but in November, 1960, she was found at home in a stuporous condition, and was admitted as an emergency.

She was thin and very cold (rectal temperature, 83°F or 28·3°C); the pulse-rate was 40 per min.; the blood-pressure was unrecordable. She moved her limbs occasionally and shivered, but no reflexes were elicited. An electrocardiogram taken immediately showed sinus bradycardia, long PR and QT_c intervals, and J deflections characteristic of hypothermia.

Investigations

Hæmoglobin 12·0 g. per 100 ml. White blood cells, 9000 per c.mm. Serum chemistry: Na, 133 mEq. per litre; K, 2·9 mEq.; Cl, 91 mEq.; HCO_3, 25 mEq.; Ca, 5·1 mEq.; phosphate, 1·4 mEq. Blood-urea, 72 mg. per 100 ml. Serum-amylase, 1225. Somogyi units per 100 ml. Blood-glucose 110 mg. per 100 ml.

Cerebrospinal fluid was normal, and so were X-rays of the chest, skull, and abdomen.

Progress

She was put to bed in a warm sideroom without extra warming, and no special therapy was given. She improved steadily as the temperature rose to normal. The serum-amylase values fell steadily (see table).

SERUM-AMYLASE VALUES IN CASE 1

Day	Rectal temperature		Serum amylase. Somogyi units per 100 ml.
	°F	°C	
1	90	32·2	1225
2	97	36·0	1080
3	98	36·6	625
4	98	36·6	..
5	98	36·6	..
6	98	36·6	475
7	97	36·0	..
8	97	36·0	200

SECOND CASE

A labourer, aged 51, was admitted on May 30, 1961. He lived with a bachelor brother who was unable to rouse him on the morning of admission and sent for the doctor. The patient had not worked for six months, because of " poor health ". In 1953 he had a partial thyroidectomy for thyrotoxicosis, and in 1957 he developed pulmonary tuberculosis which was successfully treated by chemotherapy. In 1958 gastroenterostomy and vagotomy were performed for a duodenal ulcer, and since then he had complained of intermittent abdominal pain, of which he had had an attack a few days before admission.

The doctor found the house damp, cold, and filthy. The patient was lying comatose on his bed, clad in shirt and pants and covered by one thin blanket. During the previous three days the weather had been cold for May, falling as low as 37°F at night. There was no sign of recent alcoholic excess or drug overdose.

The patient was a well-built man, weighing 11 stone. On admission, his skin was cold and dry, but its texture was normal and there were no features suggestive of myxœdema. Rectal temperature was no higher than 80°F (26·6°C). Respirations were slow and shallow (10–12 per min.), no peripheral pulses could be felt, and the systolic blood-pressure was 85 mm. Hg. The heart sounds were not audible, the pupils did not react, and no tendon reflexes could be obtained. There were no signs of trauma and there was no distinctive fœtor.

Investigations

Serum chemistry: Na, 128 mEq. per litre; K, 3·3 mEq.; Cl, 92 mEq.; HCO_3, 14·5 mEq.; Ca, 3·9, mEq.; phosphate, 5·1 mEq. Blood-urea, 110 mg. per 100 ml. Blood-glucose 120 mg. per 100 ml.

X-rays of the chest and skull were normal.

Electrocardiography (fig. 1)

There was sinus bradycardia (30 beats per min.); PR measured 0·24 sec., QT_c 0·54 sec. A very tall and wide J wave was present in all leads except V_2, directed upward in leads I, II, III, aVL, AVF, and V_3–V_6, and downward in leads a VR

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and V_1. In leads V_4 and V_5 the J wave was as tall as the R wave and its duration was 0·24 sec. The T wave was inverted in all leads except V_2.

The record was pathognomonic of severe hypothermia.

Serum-amylase

Time	*Serum-amylase (Somogyi units per 100 ml.)*
On admission	4600
After 6 hours	4600
After 10 hours	4600

Progress

We thought it unwise to raise the temperature rapidly; so the patient was nursed in bed with normal bedclothes and with hot water bottles. But he remained comatose; the rectal temperature did not rise above 80°F (26·6° C); and he died eleven hours after admission.

Postmortem Findings

Necropsy was performed eleven hours after death. There was very little subcutaneous fat and the main abnormality was a hæmorrhagic exudate extending transversely across the posterior abdominal wall between the upper poles of both kidneys. No fat necrosis was seen and no disturbance of the gross pattern or texture of the pancreas. All chambers of the heart were dilated, and, besides a few epicardial petechiæ, there was a fresh hæmorrhage 1 cm. × 1 cm. in the right ventricular muscle just below the pulmonary valve. Histologically this was not associated with myocardial necrosis and the coronary vessels were healthy. The portion of thyroid gland remaining was adequate in bulk and normal histologically. The gastroenterostomy seemed structurally sound and there was no duodenal ulcer.

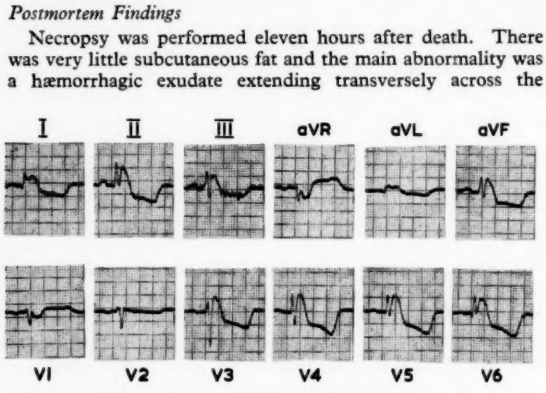

Fig. 1—The electrocardiogram of patient 2.
The bradycardia, widened PR and QT_C intervals and the conspicuous J wave with inversion of T wave are together characteristic of severe hypothermia. Note the resemblance of left chest leads to the experimentally obtained epicardial records of fig. 3. Changes as severe as this are rare in spontaneous hypothermia.

The pancreas (fig. 2) showed a recent and generalised infiltration of the interstitial tissues by polymorphonuclear leucocytes. There were also many red blood-cells, but the glandular acini were well preserved and showed a surprising lack of necrosis. The pancreatic ducts were normal. Two arterioles in one section showed partial necrosis of the wall with some fresh thrombus attached over the necrotic segment. These appeared to be a result rather than the cause of the pancreatitis. Other organs were normal.

Discussion

Both these patients had hypothermia and both had biochemical evidence of pancreatic necrosis. Further, the pancreas of the patient who died showed widespread infiltration of the connective tissue with inflammatory cells: macroscopically this had resulted in a spreading hæmorrhagic œdema of the structures of the posterior abdominal wall. That the hypothermia caused the pancreatic lesion would be in accord with experimental studies in animals (Kayser 1957) and necropsy evidence in other cases of accidental and therapeutic hypothermia. Though it might be argued that the attacks of abdominal pain were the result of pancreatitis, and that the second patient's hypothermia followed an attack, the histological appearances do not support this explanation. The changes were different from those usually seen in other forms of pancreatitis: in particular, there was no evidence of damage to glandular structures and no fat necrosis.

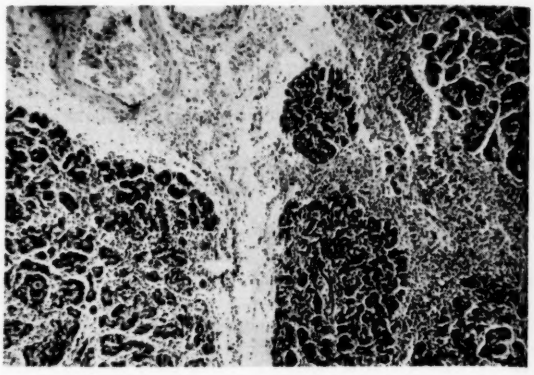

Fig. 2—A representative section (×50) of the pancreas showing hæmorrhage and leucocyte infiltration. The acini are well preserved. Two arterioles show partial necrosis of their walls.

A further point of interest is the cause of the hypothermia in these patients. One was old, but both were found indoors; and they had not been lying unattended or wet for a long period. The hypothermia sometimes seen in patients with steatorrhœa (Dent et al. 1961) may be partly due to lack of subcutaneous fat, which makes the patient more susceptible to the effects of cold; and it should be noted that our first patient was thin and the second, though muscular, had little subcutaneous fat. The first patient had undergone gastric resection, which often leads to loss of weight. In the second patient

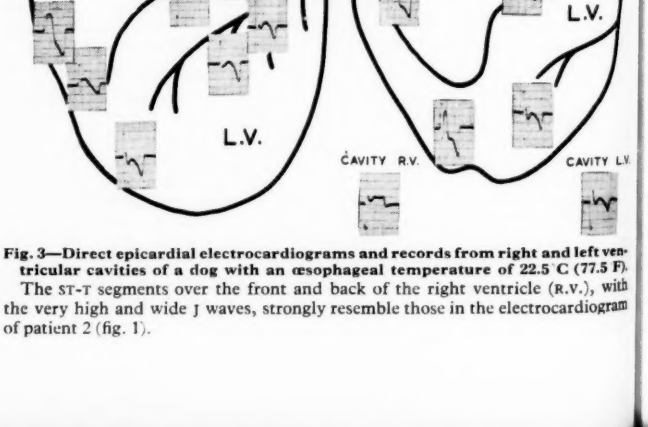

Fig. 3—Direct epicardial electrocardiograms and records from right and left ventricular cavities of a dog with an œsophageal temperature of 22.5° C (77.5 F).
The ST-T segments over the front and back of the right ventricle (R.V.), with the very high and wide J waves, strongly resemble those in the electrocardiogram of patient 2 (fig. 1).

recurrent bouts of abdominal pain, tuberculosis, and a gastroenterostomy with a poor response could explain the lack of subcutaneous fat.

It would be useful to know which hypothermic patients will develop pancreatitis. Presumably the lower the temperature the likelier is this complication. Good ancillary evidence about the severity of the hypothermia can be obtained from the electrocardiographic changes, which have now been described in both accidental and deliberately produced hypothermia (Emslie-Smith 1956, 1958, Emslie-Smith et al. 1959). In our second patient these changes were unusually severe for spontaneous hypothermia. The very high and wide J waves which were seen in his tracings, are recorded most often from animals exposed to very low temperatures (fig. 3), and they suggest a profound hypothermic change.

Our first patient survived, without vigorous rewarming. Survival is rare when hypothermia is severe enough to produce coma, and since death commonly follows vigorous rewarming (Rees 1958) and is attributed to cardiac failure or pneumonia, the best plan may be to nurse patients in bed at room temperature without added warmth. When initial serum-amylase values are high, further estimates may be a useful means of following the patient's progress.

Though the exact nature of the relation between pancreatitis and hypothermia is not clear, the association should be borne in mind; for it may be partly responsible for the poor prognosis in accidental hypothermia.

Summary

Two patients with accidental hypothermia showed biochemical evidence of pancreatic dysfunction. One of them died and there was histological evidence of pancreatitis.

We are grateful to Dr. C. C. Booth for permission to study and record the details of the first patient. We also thank Prof. T. Hewer for his help with interpretation of the pathological findings.

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RADIATION NEPHRITIS

A Long-term Study of 54 Patients

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RADIATION nephritis may follow the inclusion of the kidneys within a therapeutic field of deep X rays. This review of the disease is particularly concerned with its clinical and pathological course and is based on a study which began in 1948 of 54 patients whose progress has been carefully followed. The features of 27 of the patients were described (Luxton 1953) at a time when the ultimate outcome in most cases was unknown. Four main presentations of radiation nephritis were then recognised: acute radiation nephritis, chronic radiation nephritis, benign hypertension, and late malignant hypertension. There has been no reason to alter this essentially clinical classification. The numbers of patients whose initial presentation comes within these four categories and those asymptomatic patients with proteinuria were:

Clinical presentation	*No. of patients*
Acute radiation nephritis	20
Primary chronic radiation nephritis	10
Benign hypertension	6
Late malignant hypertension	5
Proteinuria	13

All the patients are adults: 49 men given abdominal radiotherapy after unilateral orchidectomy for malignant testicular tumours, and 5 women given abdominal radiotherapy after operation for ovarian cancer.

Acute Radiation Nephritis

After irradiation there is a latent period of six to thirteen months before symptoms of renal involvement arise. Towards the end of the latent period, however, clinical examination may reveal proteinuria, raised blood-pressure (B.P.), anæmia, and cardiac enlargement (best detected in X-ray films). Symptoms develop slowly at first but patients are usually incapacitated within four weeks. Early symptoms are œdema, dyspnœa on exertion, hypertensive headache, and nocturia; later symptoms include nausea and vomiting, lassitude, and drenching sweats; the syndromes of left ventricular failure, congestive heart-failure, hypertensive encephalopathy, and chronic uræmia may arise. Œdema is not always a feature; it is commonly confined to the legs but in severe cases it is generalised and associated with serous effusions. A pronounced anæmia is usual, normochromic and normocytic in type, and resistant to any treatment other than blood-transfusions; although it is attributed to concomitant renal failure it is often more severe than the degree of uræmia alone would warrant. The urine may contain a few red corpuscles and epithelial, hyaline, and granular casts. Gross hæmaturia is not seen but proteinuria is considerable. The blood-urea is moderately raised.

Hypertension and Malignant Hypertension

Although not invariably present during the early weeks, hypertension always appears at some stage. The B.P. is commonly at its highest within six months after the first symptom but in half the patients who survive the acute phase of the disease it returns to near normal within two years. A remarkable feature of acute radiation nephritis is that almost half the cases show the syndrome of malignant hypertension, and in a few the malignant phase resolves without specific treatment.

Prognosis

The immediate prognosis in acute radiation nephritis is related to the occurrence of malignant hypertension. Of the 20 patients in my care, 8 had malignant hypertension, of whom 6 died within three to twelve months. 2 patients with malignant hypertension recovered spontaneously: 1 died six years later in chronic renal failure, but the other is alive and at full work twelve-and-a-half years after, though he has signs of chronic renal damage.

In the present series, signs of a poor immediate prognosis included generalised œdema, retinitis, and a blood-urea over 100 mg. per 100 ml. during the first three months. Apart from malignant hypertension, the B.P. alone was not a trustworthy prognostic index. Individual features of no prognostic importance were the latent period and the age of the patient.

From this series of cases it is now not unreasonable to estimate the ultimate prognosis in acute radiation nephritis. Of my 20 patients, 10 have died from the effects of renal irradiation. Of these, 6 died from malignant hypertension within twelve months after their first

symptoms and 3 died of chronic renal failure seven to eleven years after the irradiation. A further patient died after four years with a cerebral lesion due to hypertension.

Of the 10 patients who have not died from the effects of renal irradiation, 1 has died with widespread metastases from her ovarian carcinoma. The remaining 9 patients are alive and active at an average interval of ten years after radiotherapy although all show evidence of chronic nephritis, the clinical features and course of which are discussed below.

Chronic Radiation Nephritis

Of the 54 patients in this series, 24 were classed as chronic radiation nephritis and are conveniently placed in two groups according to the mode of development:

1. *Primary chronic radiation nephritis.*—Examination of patients who had been subjected to X-irradiation involving both kidneys to a dose above 2300r revealed 10 with proteinuria and other evidence of chronic nephritis.

2. *Secondary chronic radiation nephritis.*—The 14 patients who survived from acute radiation nephritis continued with signs of chronic renal damage.

Some patients in both groups were symptom-free for years, except perhaps for nocturia and loss of energy, but others progressed steadily to a fatal chronic uræmic state.

The common urinary abnormalities were proteinuria, the presence of casts (granular, epithelial, and hyaline), and a continued deficiency in concentration. In the more severe cases, anæmia, azotæmia, and defects in renal function were revealed by the standard tests. 9 patients (2 of the " primary " type of chronic radiation nephritis and 7 of the " secondary " type) were normotensive for an average period of eight years—a fact which no doubt contributed to their survival.

A further feature of interest was the long duration of chronic uræmia; 3 patients maintained a blood-urea between 100 and 250 mg. per 100 ml. for four years before their death. Anæmia was severe in those who progressed to fatal chronic uræmia and blood-transfusions were necessary at intervals of six months or so.

Prognosis

Of the 10 patients with primary chronic radiation nephritis 3 have died in chronic uræmia at an average interval of seven-and-a-half years after irradiation, and 1 of further malignant disease after eleven years. Ten years after irradiation 2 patients show a slowly diminishing renal reserve and 3 patients are in a stationary state of compensated renal failure. The remaining man developed malignant hypertension ten years after renal irradiation.

Of the 14 patients with secondary chronic radiation nephritis, 3 have died in chronic uræmia at an average interval of ten years after irradiation, 1 died of a cerebral vascular lesion at four years, and 1 died of recurrent malignant disease. 9 patients are leading normal lives at time intervals up to twelve years after radiotherapy, and although 5 have impaired renal reserve and/or hypertension, the remaining 4 show only proteinuria. Such small numbers are no safe guide, but it is possible that the ultimate prognosis in patients who survive acute radiation nephritis is rather better than in those in whom chronic radiation nephritis develops insidiously.

Benign Hypertension

6 patients presented initially as " benign hypertension ", the main signs being hypertension and variable proteinuria. Routine renal-function studies were normal. Time has shown the hypertension to be not so " benign ", however, for 2 patients died in congestive heart-failure at intervals of five and fifteen years after radiotherapy, and 1 other developed malignant hypertension eleven years after irradiation. The remaining 3 patients have had the " benign " hypertension syndrome nine, eleven, and thirteen years respectively after radiotherapy.

Proteinuria

13 patients without symptoms but with proteinuria were observed for periods of five to nineteen years (average eleven years) after radiotherapy. The proteinuria was intermittent in 7 patients and was sometimes in small amounts only. Although standard renal-function tests were normal, these men seemed to have a latent nephritis with impaired renal reserve, as indicated by occasional elevations of the blood-urea for no obvious reason. Stress accentuated this feature: 1 man had received abdominal radiotherapy in 1942 (3000r in fifteen days) and in 1954 required appendicectomy, the operation being associated with vomiting. His blood-urea rose to 340 mg. per 100 ml., returning to 85 mg. per 100 ml. within five days and has subsequently remained within the normal range. At present (1961) he has slight proteinuria and the B.P. is 170/90, and blood-urea 21 mg. per 100 ml.

Some subjects are more susceptible to irradiation than others—just as are some tumours. It seems that in these subjects renal irradiation within the " therapeutic " range may provoke nephritis or may produce permanent renal injury without overt nephritis. The ultimate prognosis may thus be assessed only in terms of decades.

Late Malignant Hypertension

Irradiation of the kidneys has a remarkable influence in sensitising the renal mechanism responsible for malignant hypertension. Of the 54 patients, 15 (28%) developed malignant hypertension sooner or later. As previously stated, in 8 patients malignant hypertension arose during the stage of acute radiation nephritis six to thirteen months after the start of X-irradiation (it might then be described as " early " malignant hypertension). In 7 other patients, however, malignant hypertension developed at intervals of from eighteen months to eleven years after irradiation and in clinical circumstances quite different from those of acute radiation nephritis. This type is described as late malignant hypertension and carries important implications in diagnosis and treatment. For this reason a detailed account of the 7 patients is to be published later, but certain general observations will be made here.

The patients were men aged 35 to 50 years, given prophylactic abdominal irradiation after unilateral orchidectomy for seminoma in a dose of 2500–3000r in twenty-five to thirty days. Both kidneys were included in the field of irradiation so that bilateral renal damage was present in all. Observations of clinical importance were:

(1) Once begun, the malignant hypertension may progress rapidly and cause death within a few weeks.

(2) Regular follow-up examination of patients with known radiation nephritis is indicated. Malignant hypertension arose in a man who had been under observation for eleven years with the " benign hypertension " syndrome. Another man with mild chronic radiation nephritis ceased to attend the follow-up clinic for business reasons; six years later he was seen with severe malignant hypertension and a blood-urea of 120 mg. per 100 ml., so that treatment was seriously prejudiced.

(3) It was important to know whether one or both kidneys were contracted. Tomographic studies of the kidney in conjunction with intravenous pyelography were useful.

Late malignant hypertension may arise when both kidneys are of normal size or when they are equally contracted. It may be precipitated by renal ischæmia in one grossly contracted kidney and relieved by excision of that kidney even when the remaining kidney shows radiation injury. Divided renal-

function studies and examination by special radiological techniques may be helpful in such patients. Especially difficult are cases in which one kidney is only moderately contracted and still functioning to some extent.

(4) Hypotensive drugs were of considerable value.

Pathological Changes in Relation to Animal Experiment and to Clinical Features

The pathology and histology of acute radiation nephritis in some of these patients have been described by Dr. Helen Russell (1953), until recently consultant pathologist at the Christie Hospital and Holt Radium Institute. In certain cases of chronic radiation nephritis the process has been aptly described by Dr. Russell as "the shrinking kidney". Fig. 1 shows the kidneys of a patient with primary chronic radiation nephritis who died thirty-eight months after renal irradiation, and fig. 2 depicts the shrivelled organs of a man who died seven years after acute radiation nephritis. Radiological evidence of this process of renal contraction is readily obtained during life (figs. 3a and b).

Of peculiar interest to this paper are the animal experiments of Wilson, Ledingham, and Cohen (1958) at the

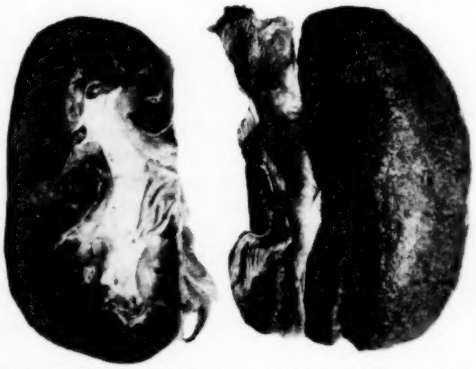


Fig. 1—Primary chronic radiation nephritis. Patient died of intercurrent disease 38 months after renal irradiation. Each kidney weighed 100 g. (normal 150 g.).

London Hospital. They studied the effects of irradiation on the blood-pressure and on the renal histology of rats which had had one or both kidneys exposed to X rays. In some experiments the kidneys were drawn out on the rats' flanks during irradiation; in others the kidneys were irradiated in situ. Of the conclusions drawn by Wilson et al. from these experiments the following are relevant here:

(1) Irradiation of both exteriorised kidneys in rats causes hypertension after a latent period corresponding to that in man.

(2) The irradiation has two distinct and independent biological effects—hypertension and interstitial fibrosis. These two effects have different time relations and may develop together or separately.

(3) Irradiation sclerosis of the kidney is a composite picture of structural damage due to the two separate processes.

(4) There is no evidence that the hypertension which follows

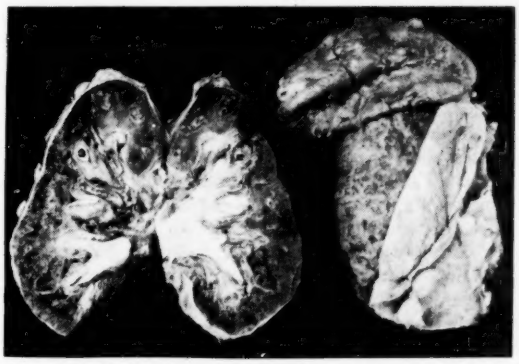


Fig. 2—Secondary chronic radiation nephritis. Acute radiation nephritis developed a year after renal irradiation; and patient died of chronic renal failure 8 years after irradiation. The kidneys were densely sclerosed: each weighed 45 g. The attached adrenal weighed 12 g.

irradiation is due to constriction of the kidney by fibrosis of its capsule, or to constriction of the renal artery by fibrosis at the kidney hilus.

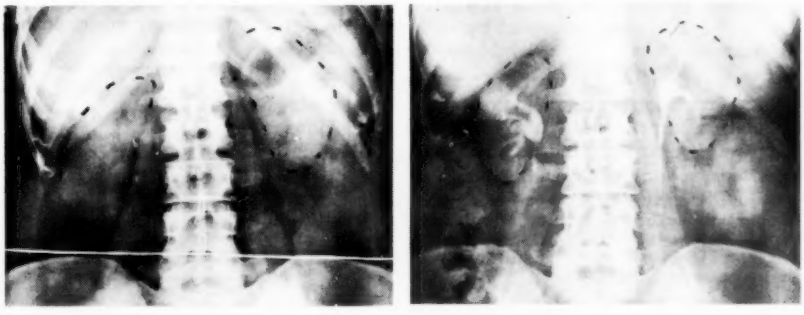
Two independent biological effects, hypertension and interstitial fibrosis, would very reasonably explain some of the pathological and histological changes in radiation nephritis in man. The syndromes seen in this series during and after acute radiation nephritis lend clinical support to this concept:

	Clinical syndrome	*No. of cases*
During acute phase	Malignant hypertension	8
Sequel to acute phase	Chronic renal failure with hypertension	6
	Chronic renal failure without hypertension	3
	Chronic hypertension without renal failure	1
	No residual hypertension or obvious renal failure	4

(2 patients with malignant hypertension recovered from acute radiation nephritis but developed other syndromes later.)

General Observations

Clinical radiation nephritis does not arise unless a large volume of one or both kidneys is directly included within therapeutic X-ray fields. So far as I can discover, other sources of ionising radiations, such as radioactive isotopes, atomic explosion, and diagnostic X rays, have not caused nephritis in man. The X-ray treatment of ankylosing spondylitis is most unlikely to cause radiation nephritis because the dose of X rays is low and most of the kidney tissue is outside the X-ray field.



(a) (b)

Fig. 3—Chronic radiation nephritis. Process of renal contraction after irradiation shown by intravenous pyelography: (a) kidney outlines before radiotherapy; (b) kidney outlines 7 years after radiotherapy.

As a tool in animal research on hypertension, X rays are valuable and may ultimately help to clarify the mechanism of malignant hypertension—and even that of essential hypertension—in man.

This series of patients may prove to be unique, because the incidence of radiation nephritis has been greatly reduced since the limit of renal tolerance to X rays was assessed (Kunkler, Farr, and Luxton 1952) and the advent of megavoltage techniques has made effective abdominal radiotherapy easier with a reduction of the renal risk. Occasional cases will continue to arise, however, for abdominal irradiation is essential to our present methods of treating testicular neoplasms and certain malignant tumours in the abdomen.

Summary

(1) Radiation nephritis may result when the kidneys are included in therapeutic fields of deep X rays.

(2) In 54 patients observed during a period of thirteen years, the initial clinical presentations were acute radiation nephritis (20 cases), primary chronic radiation nephritis (10 cases), benign hypertension (6 cases), late malignant hypertension (5 cases), and proteinuria (13 cases).

(3) In acute radiation nephritis the immediate prognosis is related to the occurrence of malignant hypertension from which, however, spontaneous recovery followed in 2 patients. After recovery from the acute phase, chronic nephritis always remains.

(4) Chronic radiation nephritis may develop insidiously (primary chronic radiation nephritis) or it may follow acute radiation nephritis (secondary chronic radiation nephritis). There is a suggestion that the ultimate prognosis is rather better in the secondary type. Patients with chronic radiation nephritis may be normotensive for several years, and may live for many months in a state of advanced chronic renal failure.

(5) Of 6 patients with the benign hypertension syndrome, 2 have died of congestive heart-failure and in 1 malignant hypertension developed after eleven years.

(6) Proteinuria alone after renal irradiation may denote a latent form of nephritis.

(7) Of the 54 patients 15 (28%) developed malignant hypertension sooner or later. " Early " malignant hypertension occurred during acute radiation nephritis. 7 patients, however, developed malignant hypertension late—that is, eighteen months to eleven years after renal irradiation. Late malignant hypertension may supervene in chronic radiation nephritis and in " benign hypertension " and it may be caused by radiation damage to one kidney.

(8) This study of the clinicopathological features and course of radiation nephritis supports the concept obtained from animal experiment that X-irradiation of the kidneys has two distinct and independent biological effects—hypertension and interstitial fibrosis.

I wish to thank my colleagues at the Christie Hospital and Holt Radium Institute for their cooperation, especially Dr. Helen Russell, Prof. Ralston Paterson, and Dr. J. Blair Hartley. The illustrations were prepared by Mr. R. Schofield in the department of medical illustration of the hospital.

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TRIAMCINOLONE IN PRIMARY PULMONARY TUBERCULOSIS

A Controlled Trial

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LYMPHATIC glandular enlargement is the most striking feature of primary tuberculous infection in childhood. The commonest affected organ is the lung, where the regional lymph-glands are close to the trachea and bronchi. Enlargement of these glands may narrow the airway either by direct pressure or because caseous material perforates the bronchial wall and partially or completely occludes the lumen. Either state may lead to segmental collapse of an area of lung, a common complication of primary pulmonary tuberculosis.

169 (19%) of 899 children with primary pulmonary tuberculosis were admitted to High Wood Hospital because of segmental lesions, and 18 (5·7%) of 317 children developed such lesions after admission (Bentley et al. 1954). Segmental lesions develop early in the disease—for example, within three months of Mantoux conversion in 50% of cases and within six months in 80%. Such lesions may persist for several months because it is unusual for hilar glands to regress until at least three months have elapsed. The commonest result is a shrunken, scarred, airless segment, and in some children bronchiectasis supervenes.

Chemotherapy with streptomycin, *p*-aminosalicylic acid (P.A.S.), and isoniazid either individually or combined does not affect the time at which the glands diminish in size, and there is some evidence to suggest that isoniazid may even increase the glandular enlargement (Bentley 1955). Steroids have been used to control allergic reactions to anti-tuberculous drugs, to reduce the associated allergic œdema in tuberculous conditions—e.g., in tuberculous pleural effusion (Aspin and O'Hara 1958)—and to limit the amount of inflammatory exudate in tuberculous meningitis (Kendig et al. 1956). They have also been given in primary pulmonary tuberculosis (Lavers and Roberts 1959) but no concurrent control group of patients was studied. It seemed, therefore, worth assessing, under controlled conditions, the effect of steroids combined with chemotherapy on hilar enlargement and segmental lesions arising during the evolution of the primary complex of pulmonary tuberculosis.

Plan of Investigation

The patients chosen were those in whom the infection seemed to be of recent onset and who had clearly defined radiological lesions and a Mantoux reaction positive at a dilution of 1 in 10,000.

A standard course of *chemotherapy* was given to all children: streptomycin 20 mg. per lb. body-weight per day, intramuscularly in a single daily dose, for twelve weeks, and oral isoniazid in a total daily dose of 5 mg. per lb. body-weight per day in divided doses 3 times daily for twelve weeks.

Alternate patients admitted to the investigation received *steroid* therapy as follows: triamcinolone orally 0·25 mg. per lb. body-weight per day for four weeks, and then 0·125 mg. per lb. body-weight per day for four weeks; the dose was then gradually reduced and stopped after a further two weeks.

The following investigations were performed:

On admission: Weight, height, general physical examination.
X-ray chest (P.A. and laterals).
Mantoux 1 in 10,000.
Erythrocyte-sedimentation rate (E.S.R.).
Serum-proteins (electrophoresis).
Blood chemistry (alkali reserve, sodium, potassium, chloride).
Gastric lavage.
Twice weekly: Blood-pressure.
Urine.
Weekly: Clinical assessment.
Weight.
E.S.R.
Fortnightly: Mantoux 1 in 10,000, 1 in 1000, 1 in 100.
Blood chemistry.
Monthly: Chest X-ray.
Serum-proteins.
Gastric lavage.

Results

During the eighteen months beginning May, 1958, 16 patients were admitted to the investigation; by alternate selection 8 were placed in the triamcinolone group and 8 in the "control" group (1 patient was later excluded from the control group because, although he had been recently in contact with his father who had active pulmonary tuberculosis and the X-ray appearances were typical, the Mantoux reaction remained negative).

TABLE I—PROBABLE DURATION OF PRIMARY COMPLEX AND ADMISSION WEIGHT

—	Case	Age	Duration of primary (wk.)	Admission weight
A. Triamcinolone	1a	7 yr. 6 mos.	..	42 lb. 8 oz.
	2a	12 4	?3–12	81 12
	3a	14 10	2	112
	4a	11 6	2 –3	57 8
	5a	2 2	3 –4	22 8
	6a	4 9	5	28 12
	7a	6 3	2	54 4
	8a	6	?6	39 8
B. Control	1b	6 9	4	41
	2b	11 6	?6	78 8
	3b	13 6	1	87 12
	4b	5 4	3 –4	39
	5b	6	2	17 12
	6b	2 3	2	24 8
	7b	2 5	2 –3	18

Table I gives the ages of the patients, the probable duration of the primary complex, and the weights on admission; and table II indicates the stage at which the E.S.R. returned to normal.

Table III gives details of the initial radiographic appearances and the time at which improvement was observed. The X-ray reports were made by the consultant radiologist (Dr. Norah Walker) who did not know whether the patients were in the triamcinolone or the control group. Table IV records the effects of triamcinolone on the Mantoux reaction.

TABLE II—RETURN OF E.S.R. TO NORMAL

—	Case	Initial E.S.R.	Returned to normal (10 mm.) (wk.)
A. Triamcinolone	1a	52	2
	2a	20	1
	3a	92	3
	4a	62	5
	5a	1	..
	6a	5	..
	7a	26	3
	8a	10	..
B. Control	1b	27	4
	2b	49	Still raised at 12 wk.
	3b	21	5
	4b	13	1
	5b	18	Not recorded
	6b	22	8
	7b	..	..

No changes were observed in the blood-levels of sodium, potassium, and chloride during steroid therapy, the alkali reserve did not vary, and no rise in blood-pressure was noted.

Changes in the serum-protein fractions were found in the steroid group; during steroid therapy the levels of γ and α_2 globulin tended to fall to normal whereas in the control group these levels remained slightly raised over the initial three months' observation.

The attempts to isolate the tubercle bacillus from gastric washings using culture and guineapig techniques were disappointing (table V). A positive result was obtained initially in 2 patients in the triamcinolone group and 3 in the control group; a positive result was obtained in a further control after 1 month's treatment.

The following case-reports illustrate the clinical and radiological features:

Triamcinolone

CASE 1a.—A boy was admitted to hospital with a history of loss of weight and listlessness for five months. He had been referred as a contact of his father who was in hospital with active pulmonary tuberculosis. Clinical examination was negative apart from a few rhonchi in the left lower lobe.

TABLE IV—EFFECTS OF TRIAMCINOLONE ON MANTOUX REACTION

Case	Initial Mantoux	Subsequent Mantoux tests
1a	1:10,000 +ve	Remained +ve 1:10,000 throughout.
2a	,,	−ve 1:1000 6 wk., 9 wk., +ve 1:10,000 11 wk.
3a	,,	−ve 1:1000 5 wk., 8 wk., +ve 1:1000 10 wk.
4a	,,	+ve 1:10,000, 2, 5, 7, wk., −ve 1:10,000. +ve 1:1000 10 wk.
5a	,,	−ve 1:1000 4 wk., +ve 1:10,000 8 wk.
6a	,,	−ve 1:1000 3 wk., −ve. 1:100 7 wk. +ve 1:10,000 11 wk.
7a	,,	−ve 1:10,000 but +ve 1:1000 4 wk.
8a	,,	Remained +ve 1:10,000 throughout.

Mantoux reaction in 1 in 10,000 dilution was positive: E.S.R. 52 mm. in 1 hour: chest X-ray revealed an enlarged right hilum and a shadow in the apical segment of the right lower lobe: three weeks after treatment began the shadow was considerably less (fig. 1).

TABLE III—RADIOGRAPHIC APPEARANCES

—	Case	Initial X-ray report	Subsequent X-ray changes		
			1 month	2 months	3 months
A. Triamcinolone	1a	Enlarged rt. hilum and shadow apical segment R.L.L.	+2	+2	+2
	2a	Enlarged lt. hilum and opacity L.U.L.	+2	+2	+2
	3a	Enlarged rt. hilum and shadow R.U.L.	+1	0	−1
	4a	Enlarged rt. hilum with shadow extending therefrom	+1	+1	+1
	5a	Patchy shadowing and atelectasis L.U.L.	+1	+1	+2
	6a	Enlarged rt. hilum with partial collapse R.U.L.	+2	+2	+2
	7a	Shadow rt. hilum extending into R.L.L.	+2	+2	+2
	8a	Enlarged rt. hilum and shadow apical segment R.L.L.	+1	+1	+1
B. Control	1b	Enlarged rt. hilar gland, shadow anterior segment R.U.L.	0	+1	+1
	2b	Enlarged rt. hilar gland, shadow R.U.L.	0	0	−1
	3b	Enlarged rt. hilum	0	0	0
	4b	Enlarged rt. hilum and shadow R.M.L.	0	+1	+1
	5b	Enlarged rt. hilum and shadow R.L.L.	0	0	0
	6b	Enlarged rt. hilum and shadow R.U.L.	0	0	+1
	7b	Enlarged rt. hilum and shadow R.M. zone	0	0	0

0 = no appreciable change. +1 = improvement. +2 = marked improvement. −1 = increase of shadow (slight).

TABLE V—ISOLATION (BY CULTURE AND GUINEAPIG) OF TUBERCLE BACILLI FROM GASTRIC WASHINGS

—	Case	Initial	1 mo.	2 mos.	3 mos.
A. Triamcinolone	1a	−	−	−	−
	2a	−	−	−	−
	3a	+	−	−	−
	4a	−	−	−	•
	5a	−	−	−	−
	6a	−	•	•	•
	7a	−	−	−	−
	8a	+	−	−	•
B. Control	1b	−	•	•	•
	2b	−	+	−	−
	3b	+	−	−	−
	4b	−	−	−	−
	5b	+	•	•	•
	6b	+	−	+	−
	7b	−	•	•	•

• = isolation not attempted.

CASE 2a.—This girl gave a history of tiredness for three months, lack of appetite, and occasional pain over the sternum. Clinical examination was negative. Mantoux reaction was positive in 1 in 10,000 dilution and E.S.R. 20 mm. in 1 hour. Chest X-rays showed an enlarged left hilum and an opacity in the left upper lobe: X-rays taken at monthly intervals showed rapid diminution in the size of the opacity (fig. 2).

Control

CASE 1b.—Two months before admission, a girl had " influenza ", her cough persisted, and in view of the presence of active pulmonary tuberculosis in the child's father further investigation was undertaken. Mantoux reaction 1 in 10,000 was positive; E.S.R. 27 mm. in 1 hour: and initial X-ray showed enlargement of the right hilar gland and a shadow in the anterior segment of the right upper lobe. Two months later (fig. 3) the picture had improved.

CASE 2b.—This girl had a sore throat eighteen days before admission to hospital, but it was not severe enough to prevent her from attending school; a week before admission a rash appeared on both shins. The skin lesions were typical of erythema nodosum; there were no abnormal signs elsewhere. Mantoux reaction was positive in 1 in 10,000 and E.S.R. 49 mm. in 1 hour. Initial X-ray showed enlargement of the right hilum and a shadow in the right upper lobe. Subsequent X-rays taken at monthly intervals showed no change, but after three months the shadow had increased in size (fig. 4).

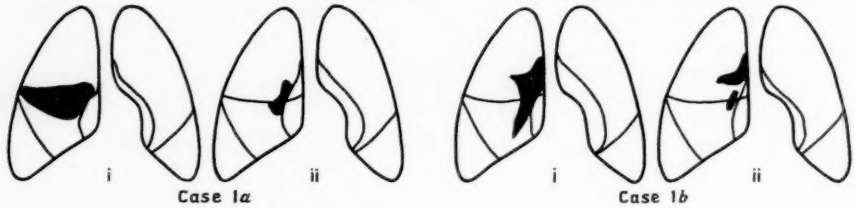
Discussion

Though the cases are few, it is clear that patients treated with triamcinolone showed a much more rapid radiological improvement than those treated with chemotherapy alone. All the steroid-treated patients showed definite, and sometimes striking, improvement within a month, whereas none of the controls showed any appreciable change in this time. Smith (1958) mentioned that about one-third of patients with glandular tuberculosis who were treated with steroids got better quickly " but there is always lurking in the back of the mind the feeling that this might have just been a case which would have done well anyway ". This trial was designed to try and bring this " feeling " to the " front of the mind " and see if it had any validity. The decline in the incidence of primary tuberculosis over the past few years has made the series much smaller than was originally planned but the difference between the two groups seems to be quite clear. Previous experience with chemotherapy has shown that little radiological change can be expected in less than three months and this emphasises that the effect of steroids seems to be a real one.

The anti-inflammatory action of steroid hormones may allow the chemotherapeutic drugs to reach the bacilli more effectively but a more important effect is probably the suppression of the allergic response to tuberculin as is shown by the reversal of the Mantoux reaction in 5 out of 8 of our patients. This will lead to reduction in the size of the glands and hence relieve pressure on the bronchi. It is important, therefore, that if steroids are to be used, they should be used early, when the allergic response is at its height.

The main danger of this form of therapy would be in a patient who was infected with organisms which were drug-resistant. Resistance of tubercle bacilli to streptomycin, isoniazid, and P.A.S. is rarely encountered in infancy and childhood and in this series the organisms which were isolated initially were sensitive to these three drugs. Experience in this hospital shows that it is very rare for resistance to develop during drug therapy, and in 2 patients (cases 2b and 6b, table v) the organisms isolated during treatment were still sensitive.

If, however, the tubercle bacilli are resistant initially because



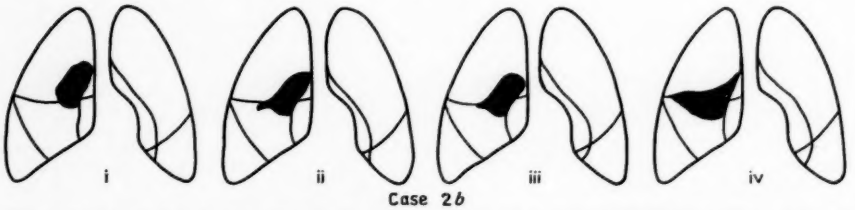


Fig. 1—Case 1a: (i) Dec. 7, 1959; (ii) Dec. 22, 1959.

Fig. 2—Case 2a: (i) Sept. 9, 1958; (ii) Oct. 8, 1958; (iii) Nov. 5, 1958; (iv) Dec. 29, 1958.

Fig. 3—Case 1b: (i) Feb. 24, 1959; (ii) April 21, 1959.

Fig. 4—Case 2b: (i) Oct. 6, 1958; (ii) Nov. 5, 1958; (iii) Dec. 11, 1958; (iv) Jan. 13, 1959.

the child has been infected by a resistant strain from an adult, there is a risk that steroid therapy would cause primary lesion to spread.

Provided that the infecting organism was drug-sensitive, steroids could play a valuable part in the treatment of primary tuberculosis when compression by glands was producing segmental collapse. They may also hasten the natural resolution of uncomplicated disease, but there is little advantage to be gained from this.

Summary

In a controlled trial of corticosteroids combined with standard antituberculous drugs in the treatment of primary pulmonary tuberculosis in children, patients treated with corticosteroids showed a much more rapid radiological improvement than those treated with chemotherapy alone, all showing definite and sometimes marked improvement in a month.

We wish to thank Dr. J. R. Wilson, of Lederle Laboratories Division of Cyanamid of Great Britain, Ltd., for a generous supply of triamcinolone (' Ledercort ').

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EFFECT OF METHICILLIN SPRAY ON STAPHYLOCOCCAL COLONISATION AND LESIONS IN A NURSERY

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METHICILLIN is very resistant to staphylococcal penicillinase, with the result that most penicillinase-positive (" resistant ") strains are inhibited by the drug (Rolinson et al. 1960). Some primary resistant strains have, nevertheless, been encountered (Jevons 1961). To our knowledge no staphylococci have acquired resistance to methicillin during treatment of patients. An increase in the prevalence of methicillin-resistant strains is not very likely as long as its use is limited to hospitals and close bacteriological control is practised.

Methicillin spray has been used in an effort to control staphylococcal infections in a maternity ward (Elek and Fleming 1960). The basis for this use was an observation that the air around places where penicillin was handled often contained demonstrable amounts of the drug (Gould 1958). This was considered an important factor in the establishment of penicillin-resistant staphylococci in hospitals. As a result of the spraying there was a reduction in the frequency of colonisation of the infants' noses, but the effect on staphylococcal lesions was not investigated. We have followed the colonisation of the infants' noses and lesions in mother, infant, and family in connection with the spraying of methicillin.

Methods

Maternity wards.—Two maternity wards (wards I and II) on adjacent floors of Aker Hospital were sprayed. The wards have almost the same size of 400 c.m. (15,000 c. ft.) and are arranged similarly. The infants are nursed in a special nursery room and brought to their mothers five times a day through the corridor for suckling. Two and four bedrooms are available for the mothers. The only connection between the wards is through the corridors and stairs. The personnel were separate except for a few trainees who were exchanged once. Only the nursery was sprayed in each ward.

The spraying.—After an introductory time of four weeks, spraying was started in ward II with 1 g. four times a day of methicillin. The spraying lasted for three weeks, but after twelve days the amount was reduced to 2 g. a day. During the following four weeks methicillin was sprayed, at the lower rate, in ward I. Observation was continued for two weeks after the termination of spraying. The technique of spraying was almost identical with that described by Elek and Fleming (1960).

Sampling.—Nose swabs were taken from the infants on the day of discharge (mostly on the fifth day), and seeded on blood and mannithol-sodium-chloride agar plates. After the completion of the investigation the isolated staphylococci were tested for sensitivity in tube-dilution tests against methicillin (Ulstrup 1960). All strains were inhibited by 5 μg. per ml. or less.

Recording of lesions.—Eight weeks after discharge from the hospital a questionary was mailed to the mothers inquiring of breast boil or mastitis (without boil) in the mother, blisters or boils (pyodermia) in the infants, and blisters or boils in the remaining members of the family since delivery. The questions could be answered " yes " or " no ". Answers were received from 463 out of 472 mothers, who gave birth to 478 infants. Ambiguous answers were corrected by a further inquiry. The lesions were listed according to week of delivery. No correction was made for the nine missing answers, nor for twin births. Nor was family size considered when lesions in family were calculated. The spraying was started on Thursdays and the groups were recorded from Mondays to Sundays.

TABLE I—WEEKLY FIGURES OF THE INVESTIGATION

—	Weeks												
	1	2	3	4	5	6	7	8	9	10	11	12	13
Ward I:													
Deliveries	23	11	16	10	23	15	15	*21*	*14*	*11*	*14*	24	26
Nasal colonisation	6	6	6	3	7	9	6	*5*	..	..	*2*	5	8
Breast abscesses	..	..	1	..	..	..	..	..	..	..	..	..	1
Mastitis	5	3	2	1	2	1	3	*2*	*2*	..	..	1	2
Pyodermia	2	..	1	..	1	1	1	..	*2*	*2*	*1*	2	2
Family boils	1	..	..	..	1	..	..	..	*2*	..	*1*	2	..
Ward II:													
Deliveries	24	15	19	12	*17*	*19*	*17*	24	13	24	15	23	33
Nasal colonisation	10	6	8	1	..	..	..	1	2	12	3	10	16
Breast abscesses	1	..	..	1	..	..	..	..	..	1	..	..	..
Mastitis	3	..	3	..	*2*	*2*	*2*	1	..	3	..	1	2
Pyodermia	..	..	1	..	*1*	..	*2*	..	..	..	..	2	1
Family boils	..	..	1	..	..	*1*	*2*	..	1	2	..	3	1

Italicised figures relate to spraying periods.

TABLE II—STAPHYLOCOCCAL CULTIVATION FROM INFANTS' NOSES

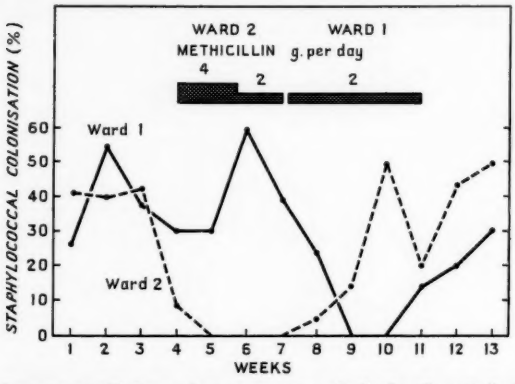
—	No spray	Spray
Growth:		
Present	125	7
Absent	240	106
Total	365	113
% positive	34	6

Results

Table I shows the weekly number of deliveries and of the corresponding colonisations and lesions recorded.

In table II the frequency of staphylococcal isolations is listed according to room treatment. During spray, staphylococci were isolated from 6% of the infants, compared with 34% during control periods. This difference is statistically highly significant.

The accompanying figure shows graphically the nasal colonisation among the infants. In ward II no staphylococci were isolated during three weeks, and in ward I two weeks were free.



Percentage of infants whose noses were colonised each week during the investigation.

Blocks indicate start and termination of spraying in each ward. Continuous line: ward I. Interrupted line: ward II.

In table III the frequencies of the recorded lesions are given. Following deliveries, during a spraying period, a frequency of 20·8% was obtained, compared with 17·6% during control periods. Apparently, therefore, the spraying had no effect on the lesion frequency.

Table IV shows that infection with type 80/81 caused lesions from 3 to 7 times as often as the other types. Since the group was small conclusions from this can only be tentative.

Discussion

Maternity-ward staphylococcal infections have long been recognised as a serious problem causing pyodermia and not infrequently more severe infections in the infants, mastitis with or without abscesses in the mothers, and family epidemics of boils. Most of these lesions, caused by infections acquired during the stay of mother and infant in the hospital, appear after discharge, and in an earlier investigation (Ulstrup and Ødegaard 1960) it was shown that lesions occurring within eight weeks after delivery are very likely to be due to hospital infection. Furthermore, a high correlation was found between occurrence of the epidemic type of staphylococcus in infants' noses and the occurrence of pyodermia in the infants and breast abscesses in the mothers. Nevertheless, it is not certain whether the mothers are primarily infected from the infant's nose during suckling or whether the infection is transmitted in some other way.

Various measures have been used for the prevention and treatment of maternity-ward staphylococcal infections. Besides improvement of the general hygiene, antiseptic prophylaxis with hexachlorophane (Gillespie et al. 1958) or triple dye (Manfield et al. 1960) and prophylactic treatment with erythromycin (De Franco 1958) have been used. Elek and Fleming (1960) found that spraying a maternity ward with methicillin had a notable effect on the frequency with which the infants' noses were colonised.

In two comparable maternity wards similar results were obtained by us during a total of seven weeks of methicillin spraying. The frequency of nasal colonisation was 6% during the spraying period compared with 34% during the control period. These results were obtained with a somewhat lower dosage (2 g. a day). A possibly more distinct effect was obtained in one of the wards where treatment was started with 4 g. a day and was reduced to 2 g. after about half the period. The frequency rose to about the prespray level soon after termination of the spraying. In contrast to this effect on the colonisation, no effect was observed on the frequency of lesions. In our hands, nasal swabbing for staphylococci during methicillin spraying of the nursery was not a reliable method for testing the epidemiological situation. Swabs were taken from the infants in the morning about ten hours after the last spraying. Possibly the infants' noses were colonised but any staphylococci present were not reached by the swab. Another possibility is that some methicillin present prevented growth on the plates, and that infecting staphylococci may have started growth in the infants' noses after discharge from the hospital. Finally, it is possible that lesions of moderate severity which dominated the period (only 5 breast abscesses) may have been due to infections acquired outside the hospital. There was no substantial epidemic at the time, although phage type 80/81 was present. It appears from table IV that this type was probably more virulent than the other types, but the figures are too small for any certain conclusions. Besides 5 breast abscesses, 22 pyodermias occurred in 478 deliveries during a period of thirteen weeks; none appeared during stay in hospital.

It is a common experience that the suppression of gram-positive organisms may favour the growth of gram-negative bacteria. In this investigation *Escherichia coli* was found in only a few instances in the infants.

No untoward effects attributable to the spraying were detected in the infants. Two nurses had slight vesiculo-eczematous lesions on the forearms at the close of the spraying period, and complained of general itching which was relieved by water shower. When attention was drawn to this symptom, some of the other nurses complained of similar irritation. After completion of the investigation all the nurses were tested with a scarification test against methicillin, but no hypersensitivity reaction was observed.

TABLE III—LESIONS IN MOTHER, INFANT, AND FAMILY WITHIN 8 WEEKS OF DELIVERY ACCORDING TO ROOM TREATMENT

—	No spray	Spray	Total
Lesions:			
Breast abscesses	5	0	5
Mastitis	33	10	43
Pyodermia	14	8	22
Family boils	12	6	18
Total lesions	64	24	88
Deliveries	363	115	478
% lesions	17·6	20·8	18·0

TABLE IV—DISTRIBUTION OF LESIONS ACCORDING TO STAPHYLOCOCCAL TYPE IN INFANT'S NOSE

—	Phage type/group							No growth
	80/81	I	II	III	V	Misc.	N.T.	
Lesions:								
Breast abscesses	1	..	..	..	1	..	1	2
Mastitis	1	1	1	1*	1	3†	1	34
Pyodermia	2	2	..	..	1	..	..	17
Family boils	3	..	..	1	..	1	..	13
None	3	25	10	22	6	25	22	289
%lesions	70	11	9	8	33	14	8	18·6

* Occurred following spray period.
† 1 occurred following spray period.
N.T. = Non-typable.

Summary

The nursery rooms of two maternity wards of Aker Hospital, Oslo, were sprayed with methicillin during a total of seven weeks. The untreated wards served as controls. The amounts of methicillin were 4 g. a day for two weeks and 2 g. a day for five weeks.

6% of the infants' noses were colonised during the spraying period, compared with 34% during the control period.

In contrast with this notable reduction in nasal colonisation, infective lesions were not reduced at all. The figures for lesions were 20·8% following deliveries during a spraying period, and 17·6% during the control periods. No effect on colonisation was detected in the untreated ward during spraying of the other.

Colonisation with gram-negative bacteria presented no problem.

No untoward effects which might be due to methicillin were observed in the infants; but two nurses, previously "skin-healthy", had small vesiculo-eczematous areas on their forearms at the termination of the spraying. There was some complaining among the personnel of general itching, but no methicillin hypersensitivity was demonstrated.

We thank our colleagues and the nurses at Aker Hospital for valuable cooperation in the investigation.

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THE ^{131}I-TRIOLEIN FAT-ABSORPTION TEST

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THE concept of "steatorrhœa" was introduced well over a century ago to describe a clinical state associated with excretion of visible globules of fat in the fæces. Later it was found that malabsorption of fat has a variety of clinical manifestations. Some of these are direct effects of insufficient absorption of fat; others may be caused indirectly by the body's lack of fat-soluble substances (vitamins, organically bound metal complexes, &c.) which are normally ingested in fat suspension.

Fat-deficiency syndromes become manifest when the fat available to the body is insufficient to maintain various metabolic processes at the normal level. But it appears increasingly probable that some of these processes depend on the availability of specific fat constituents needed in the biosynthesis of particular tissue components—liproproteins, cell membranes, &c. Hanahan and Blomstrand (1956) and Mead and Fillerup (1957) have shown that incorporation of fatty acids into lipids depends on chain length and degree of saturation.

If there is not enough of the right kind of fat, either because absorption is impaired, or because some metabolic process (e.g., deposition or oxidation) consumes an abnormal amount, deficiency syndromes may develop. Thus the same kind of deficiency syndromes may be caused either by inadequate absorption of fat or by its defective utilisation.

Reflecting the early concept of "steatorrhœa", the analytical techniques first developed were methods of chemical determination of fæcal fat. The most exact of these are the "fat balance" in human subjects, and the Cori technique (involving excision of the whole gastro-intestinal tract) in animal studies. "Fat balance" determinations, besides being complex and time-consuming, have several inherent sources of error. As Hendry (1960) points out, the errors of sampling can be considerable. Furthermore, the fæcal fat may not all be derived from ingested fat: Sperry (1929) found that up to 40% might be formed by bacterial synthesis. The fact that gut-sterilising drugs such as sulphonamides and tetracyclines will sometimes considerably reduce the percentage of fat in the fæces points strongly in the same direction.

Again, there is evidence that intestinal mucosa can actively secrete lipids into the small intestine (Sperry and Angevine 1932, Lewis and Partin 1954). From experiments with ^{14}C-labelled palmitic acid Tidwell et al. (1956) conclude that probably an appreciable amount of lipid is secreted into the alimentary tract during the period of fat absorption, and that the secreted lipids may be partly reabsorbed and partly excreted. Furthermore, the chemical method of analysis of fæcal fat cannot show whether any of the constituents in the mixture of natural fats have been selectively absorbed or rejected.

Determination of the amount of lipid remaining in the alimentary tract after feeding fat (Cori technique), and determination of the fat excreted in the fæces ("fat balance"), are direct measurements of fat absorption. There are several ways of measuring fat absorption indirectly, by following the rate at which fat appears in the blood-stream (chylomicrography; radioactivity of labelled fat), or by estimating the oxidation of labelled fat as shown by the rate of excretion of $^{14}CO_2$. These indirect methods are influenced by fat absorption as well as by fat utilisation (degradation, deposition, and mobilisation). From a comparative study of direct and indirect methods at present in use, Tidwell et al. (1956) conclude that all the indirect ones seem to "reflect the rate of absorption of the fat fed".

The discovery by Stanley and Thannhauser (1949) that ^{131}I-labelled olive oil can be used for studying fat absorption has given rise to much work.

The stability of the C-I bond in the labelled triolein was studied by Balint et al. (1960). They found it stable at body temperature in the presence of gastric and duodenal juice, pepsin, pancreatin, and physiological saline solution. Intracellular enzymes in the intestinal wall, and in the liver, removed 10–20% of the iodine from the labelled oil in two hours, and oil in contact with fæces lost 5% in twenty-four to forty-eight hours. In a study in which ^{131}I-labelled oleic acid and ^{14}C-labelled stearic acid were used simultaneously in experiments on animals, Van Handel and Zilversmit (1958) also found that the C-I bond is broken at a similar rate. Further, they point out that in the liver phosphatides the ^{131}I activity of the labelled oleic acid is very much smaller than the ^{14}C stearic-acid activity. They also found that, determined chemically, ^{131}I-labelled triolein given intravenously as an emulsion disappears from the blood at the same rate as neutral fat. This was also found by Turner (1958).

Efforts have been made to use ^{131}I-labelled fat for the clinical diagnosis of fat malabsorption syndromes

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(Baylin et al. 1955, Beres et al. 1957, McKenna et al. 1957, Grossman and Jordan 1958, Isley et al. 1958, Kaplan et al. 1958, Mohamed and Hume 1959). But the experimental provisions, and particularly the feeding and the assay conditions, used by the various groups of investigators differ so much that their results can hardly be compared.

In our study the conditions for administration of the test meal resemble normal feeding conditions. In the preparation of the meal " emulsifying agents " have been strictly avoided. Frazer (1958) and others have shown that surface reactions play an important role in fat absorption. In pilot experiments we found that quantitative volumetric dispensing of the viscous labelled oils requires particular care: capillarity and adhesion to glassware (especially with small-bore pipettes) make it necessary to wash out the pipettes repeatedly with inactive oil, using very low rates of flow.

Methods

Preparation of the Meal

The stock solution of ^{131}I-labelled triolein was obtained from the Radiochemical Centre, Amersham. This material is iodinated to 30–40% of the total iodine number, and was supplied to us as 10 mC of iodinated triolein dissolved in 10 ml. of olive oil *B.P.* From this stock a working solution containing approximately 25–50 μC per ml. was prepared by dilution in olive oil.

In preparing a meal, 120 ml. of skimmed milk was placed in the head of a blender,[1] followed by an amount of olive oil *B.P.*[2] which, together with the requisite amount of the active working solution, totalled 15 ml. The inactive olive oil when added to the skimmed milk formed an immiscible layer on the surface. The required volume of the working solution was then very slowly added from a pipette into one sector of this layer, after which the pipette was twice washed out with the inactive olive oil from a sector as far as possible removed from the one into which the active olive-oil solution was added. In this way the amount of activity remaining in the pipette was less than 1–2% of the total activity used for the preparation of the meal.

By successive dilutions of the active olive-oil solution with petroleum ether, two standards were prepared, one of 1/1000, and one of 1/100 of the activity of the meal per millilitre. 1 ml. of the first standard was made up with petroleum ether to 5 ml., and was used as a reference for blood-activity measurements carried out in a well scintillation counter.[3] 1 ml. of the second standard was made up with skimmed milk to 150 ml., and placed in a container identical with those used for fæces samples; it was then used as a reference for fæcal-activity measurements carried out with an annular array of Geiger counters.

It is important that the meal should be as acceptable as possible, and several alternative flavourings were tried in non-active mixtures before sweetened coffee was adopted as the best. Most patients find this not unpleasant and those who dislike it usually tolerate it without difficulty. A teaspoon or two of coffee extract and a similar quantity of sugar was added after the transfer of the olive oil to the milk, and the mixture was then homogenised at 12,000 r.p.m. for three minutes. The test-meal thus prepared was given to the patient with a minimum of delay.

Thyroid uptake of liberated ^{131}I was blocked by administering five drops of Lugol's solution on each of the two days preceding the test and on the day of the test. The patient fasted overnight and ingested the labelled-fat meal at about 9 A.M.: thereafter he remained fasting until about noon, when food and fluid in normal quantity were allowed. Venous blood was usually drawn at two, three, four, and six hours after the ingestion of the meal, but in a few cases these times were varied. The blood was put into bottles containing ammonium/potassium oxalate anticoagulant. Fæces were collected twenty-four-hourly for radioactive assay until the activity had fallen to background levels.

1. ATO-mix 800. Measuring and Scientific Equipment, Ltd., London, S.W.1.
2. Hopkin & Williams, Ltd., Chadwell Heath, Essex.
3. EKCO Electronics, Ltd., Southend, Essex.

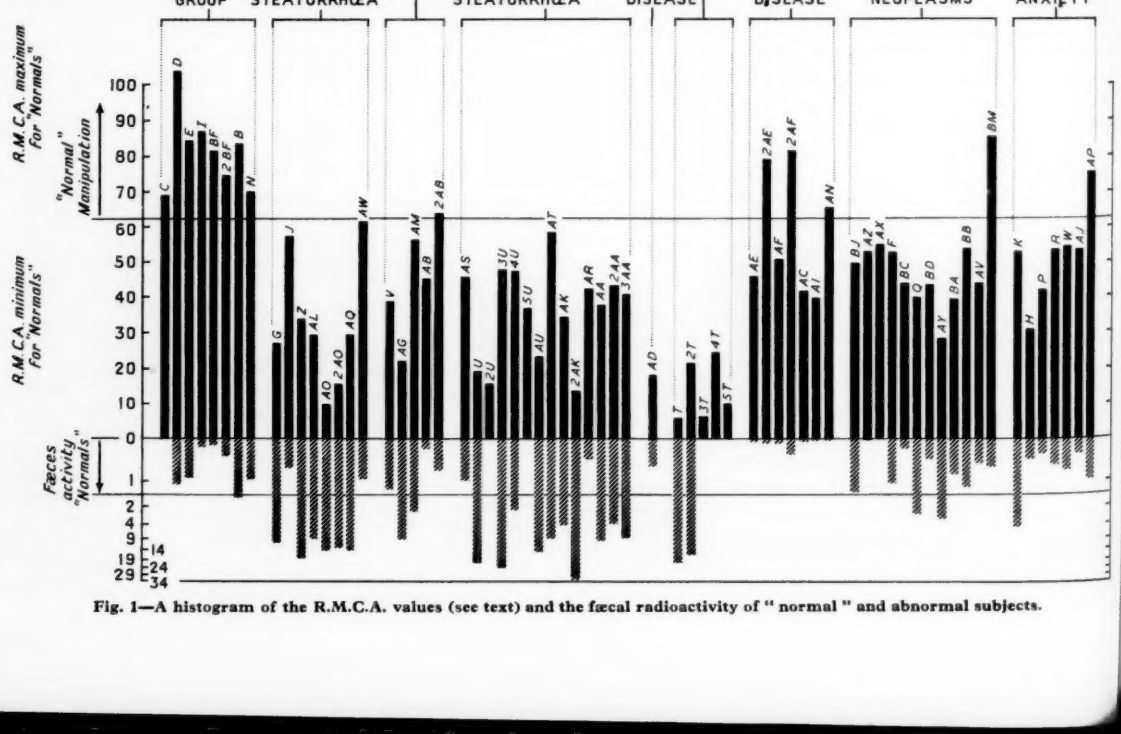

Fig. 1—A histogram of the R.M.C.A. values (see text) and the fæcal radioactivity of " normal " and abnormal subjects.

Where the meal contained a level of activity in the range of 25–50 μC, 1 ml. of whole blood was pipetted very slowly into a glass-stoppered counting-tube containing 4 ml. of saponin solution, the pipette being washed out with the saponin solution. Where the meal activity was in the range of 5–25 μC, a small quantity of saponin powder was added to the whole blood, and 5 ml. of the hæmolysed blood was transferred to the counting-tube. From the measured activity of these samples, and the activity of the meal/1000 standard, the proportion of the meal was calculated per millilitre of the peripheral blood at the time of the sample being withdrawn from the patient. The total blood-volume was estimated from a height and weight nomogram (Hicks et al. 1956), and hence the proportion of the meal in the circulation was calculated.

Distribution of Labelled Lipids in Blood and Fæces

Precipitation of the proteins and the lipoproteins, and simultaneous extraction of the lipids, was accomplished with a mixture of methylal and methanol (4/1, v/v), and the extracted lipids were studied by chromatographic and other biochemical methods which will be described elsewhere.

Determination of Free Iodine

The amount of ^{131}I removed from the labelled substance by metabolic action was determined in the extracts of blood and fæces by shaking the solutions for five minutes with 500 mg. of de-acidite FF.[4] After the resin had been washed repeatedly with water, or with the particular solvent of the various extracts, the activity of both the resin and the solution was counted. Free ^{131}I was found to vary between 2 and 4% of the whole-blood activity at times up to six hours after ingestion of the meal.

Distribution of Activity between Red Cells and Plasma

After a count of the whole blood, it was centrifuged. The separated red cells were washed three times with physiological saline, the washings being added to the plasma and the solution counted. The washed cells were then hæmolysed with saponin, and the suspension also counted. The activity of the whole blood, of the cells, and of the plasma was then expressed as a percentage of the activity of the ingested meal.

Cases Studied

81 determinations were performed on 65 subjects of both sexes (ages 14–77). The series included a "normal" group of hospital patients without evidence of diseases known to be associated with malabsorption syndromes. The rest of the series were patients with idiopathic, pancreatic, postgastrectomy and postpancreatectomy steatorrhœa, Crohn's and Hodgkin's disease, various malignant neoplasms, and a group with weight-loss associated with mental depression and anxiety. At the time the test was made, the clinical diagnosis was normally known only to one of us (E. S. W.).

Results

Fig. 1 groups the results according to the clinical diagnosis. In the "normal" subjects neither clinical conditions nor investigation had implicated fat absorption or utilisation.

Fig. 2 summarises the results of the radioactive triolein test and of the chemical fat-balance studies in "normal" subjects. Under our experimental conditions not more than about 1·5% of the activity of the meal should appear in the fæces, but percentages up to about 3 are of uncertain significance.

The dotted line in fig. 2 represents the mean circulating radioactivity, and the shaded area one standard deviation on either side of the mean. Comparison of one person with another is difficult because of the irregular shape of the curves; so in each case the area enclosed by the curve, the abscissa, and the six-hour ordinate was calculated and

4. Permutit Co., Ltd., London, W.4.

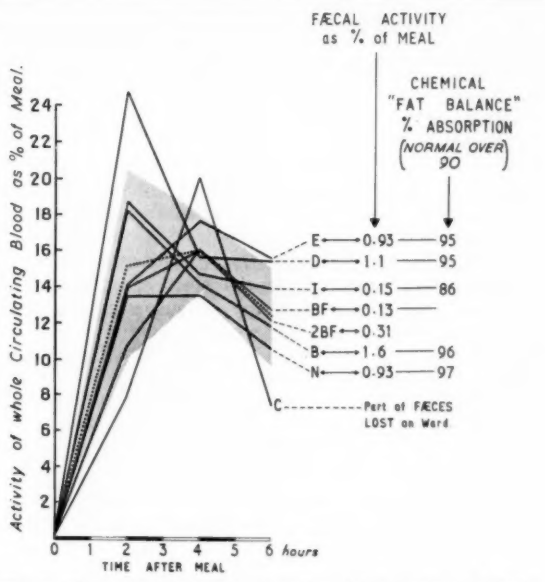
FÆCAL ACTIVITY as % of MEAL
CHEMICAL "FAT BALANCE" % ABSORPTION (NORMAL OVER 90)
Activity of whole Circulating Blood as % of Meal.
TIME AFTER MEAL
hours
E 0·93 95
D 1·1 95
I 0·15 86
BF 0·13
2BF 0·31
B 1·6 96
N 0·93 97
C Part of FÆCES LOST on Ward

Fig. 2—Blood radioactivity, fæcal radioactivity, and results of the chemical fat-balance studies in 8 "normal" subjects.

expressed as a percentage of the similar area bounded by the curve of the mean normal plus one standard deviation (upper limit of the shaded area). This percentage was called the relative manipulation curve area (R.M.C.A.). In each case it was calculated by cutting out the relevant areas and weighing them.

Reproducibility

Some cases were tested more than once. Whenever the curve of blood activity was abnormal on the first test it remained abnormal on subsequent tests. Similarly, in all cases where the fæcal activity was above the normal range repetition of the test produced consistent results. One case was investigated twice, at an interval of seven days (BF and 2BF), and the blood curves and fæcal activities were constant.

Distribution of Activity between Red Cells and Plasma

The distribution of activity between the labelled lipids in the plasma and the red cells was examined in a "normal" subject (table I).

Statistical Analysis

Tables II and III summarise the mean values of blood radioactivity in the normal group and in the groups with fat-malabsorption syndromes.

Discussion

Doubt has been cast on the clinical usefulness of the ^{131}I-triolein test, and the present study includes an attempt to eliminate the factors possibly responsible for unreliable results. The non-physiological nature of the labelled fatty meal employed by many workers is undesir-

TABLE I—RELATION OF THE ACTIVITIES OF LABELLED LIPIDS CONTAINED IN PLASMA AND RED CELLS OF A "NORMAL" SUBJECT

Time after ingestion (hr.)	Whole blood (% of meal)	Plasma (% of meal)	Red cells (% of meal)
1	8·39	6·51	0·06
2	18·18	14·92	0·29
4	14·20	11·46	0·22
6	11·77	9·29	0·16
8	9·16	6·83	Sample lost
25	3·35	2·34	0·02

TABLE II—RADIOACTIVITY OF THE BLOOD OF THE " NORMAL " SUBJECTS

Hours after meal	Mean blood activity (%)	Standard deviation	Variance
2	15·18	±5·25	192·88
4	15·94	±2·06	29·88
6	12·42	±2·66	49·64

able. We have rigidly standardised the experimental arrangements and have eliminated such additions to the meal as emulsifying agents.

It was thought possible that coexistence of other diseases might affect the results when the ^{131}I-triolein test was used for investigation of suspected fat malabsorption. Our preliminary work shows that it may do so, and this has contributed to our decision to publish results from relatively small series.

The sources of error in chemical fæcal-fat determinations are well known, and it therefore seemed inadvisable to use such determinations as a standard of comparison for the results of the radioactive test. The clinical value of our results was assessed by comparison with the diagnosis reached from the history, examination, laboratory tests, and therapeutic response.

TABLE III—DIFFERENCE BETWEEN THE MEAN VALUES OF BLOOD RADIOACTIVITY IN " NORMAL " SUBJECTS AND THOSE WITH THE CONDITION SHOWN.

Comparisons of the "normal" group and the group of	Hours after meal	Mean blood activity (%)	Variance (d)	"Student's" t	Probability (P)
Postgastrectomy steatorrhœa	2	6·46	39·12	4·43	>0·001
	4	6·98	43·57	7·06	>0·001
	6	6·13	37·72	4·56	>0·001
Idiopathic steatorrhœa ..	2	4·43	66·42	4·65	>0·001
	4	7·80	97·09	5·25	>0·001
	6	7·01	35·17	4·10	0·01–0·001
Crohn's disease	2	4·07	9·25	4·01	0·01–0·001
	4	9·87	35·08	3·89	0·01–0·001
	6	8·42	34·43	2·25	0·05–0·01
Hodgkin's disease	2	5·66	36·95	3·19	0·01–0·001
	4	12·38	50·79	2·02	>0·05
	6	8·04	6·34	2·98	0·05–0·01
Malignant neoplasms ..	2	6·90	73·08	4·73	>0·001
	4	10·26	67·67	5·36	>0·001
	6	8·58	44·92	4·72	>0·001
Depression and anxiety ..	2	7·62	43·86	3·60	0·01–0·001
	4	10·36	37·50	5·10	>0·001
	6	8·90	27·50	2·33	0·05–0·01

Although pilot experiments on the distribution of radioactivity between the red cells and plasma (table I) have shown that, under our experimental conditions, the red cells contain only a negligible proportion of that in the whole blood, it is undesirable to carry out assays on plasma. Representative aliquots for analysis are hard to obtain, because unevenly distributed fat globules, which adhere to glass surfaces, are formed during centrifuging. This effect has been observed also by Van Handel and Zilversmit (1958).

The blood radioactivity curves represent the kinetic state of balance between the absorption of fat into the blood and its removal therefrom by metabolic processes. These curves may thus be regarded as reflecting overall fat manipulation by the body, and we have called them " fat manipulation curves ". Quantitative comparison between the curves is difficult because of their irregular shape; so (as already described) we compared the areas enclosed by the curves.

Certain features of fig. 1 require further comment. The test appears to reflect clinical improvement, as shown by patients J and AW who were in remission when the test was carried out; patient AB in whom the test was repeated (2AB) after operation for Crohn's disease; and cases AE and AF in whom the test was carried out before radiotherapy for Hodgkin's disease and during remission after the treatment (2AE, 2AF). The results U to 5U represent successive tests over a period of five months, the trend of the R.M.C.A. values agreeing well with the clinical response to supportive treatment.

Patients with malignant disease and those with depressive states gave results in which typically the fat absorption was normal but the fat-manipulation curve was abnormal. The series T to 5T shows successive results extending over four months. Although in this case clinical response to substitutive treatment following pancreatectomy was good, the R.M.C.A. remained low, possibly because of the malignant disease for which the operation had been performed. Some groups of disease are exceptions to the typical pattern, and it is in these that further investigation is particularly called for.

The statistical analysis shows that the differences in the levels of blood radioactivity in the group of normal subjects and in those with steatorrhœa is highly significant ($P=0·01–0·001$). Although the difference is significant at each of the standard times at which a venepuncture was performed (two, four, and six hours after the meal), the test is likely to be more reliable if the curve of blood radioactivity is plotted and the R.M.C.A. value calculated for each case.

Summary

1. The ^{131}I-triolein test is discussed in relation to other tests for fat malabsorption. A standardised procedure for the preparation and administration of the labelled meal is described.

2. A new method of presenting measurements of blood-radioactivity is described.

3. Results of using the test on 81 occasions in 65 patients are compared with the clinical assessment based on the history, examination, laboratory tests, and therapeutic response.

4. In the 34 cases where fat absorption was in question the result of the test agreed with the final clinical diagnosis.

5. Both depression and malignant disease appeared to affect the test results.

6. The test was found to give satisfactorily reproducible results.

We wish to thank the physicians and surgeons of the Middlesex Hospital for permission to study patients who were under their care. We also wish to thank Prof. A. Neuberger, F.R.S., Dr. G. D. Hadley, and Dr. J. D. N. Nabarro for their helpful suggestions in reading the manuscript.

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ANTERIOR-CHAMBER IMPLANTS WITH BUILT-IN STENOPÆIC APERTURE *

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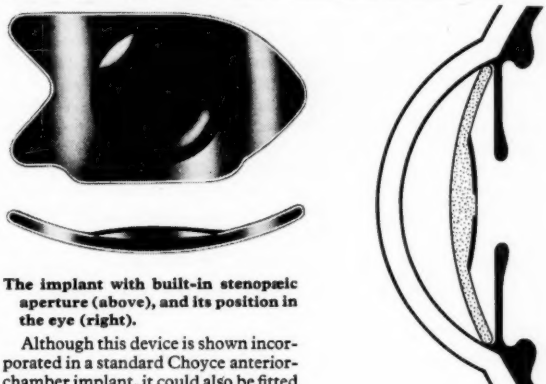
THE insertion of an anterior-chamber implant to correct aphakia can reduce the spherical error to within ±1 D.S. in 95% of cases (Choyce 1960a). An average residual cylindrical error, of the order of −2 D.C. axis within 30° of the horizontal, has remained; and most patients require an average reading addition of +3 D.S. The astigmatism probably results from the healing of the temporal incision required for the insertion of the implant (Choyce 1961); but in some cases I observed that the residual cylindrical correction and the necessary reading addition were very much less than the average. This was especially so in patients with an unusually small pupil. Two other observations suggested that a modification of the implant might intentionally increase the depth of focus and diminish the residual cylindrical correction instead of leaving this to chance:

A woman of 35 had been born with comparatively slight congenital cataracts. After thyroidectomy for thyrotoxicosis at 25, parathyroid tetany developed. The disturbance of calcium metabolism caused rapid progression of the cataracts, which were needled seven times in the right eye and six times in the left. With +12 D.S. right and left her visual acuity was 6/6 right and left. A reading addition of +3 D.S. enabled her to see N.5 at 20 cm., but for various reasons she could not tolerate this spectacle correction. For a time she wore contact lenses, but eventually she had to give those up because they caused recurrent epithelial erosions of the cornea. Bilateral anterior-chamber implants were then inserted, with the unexpected but highly satisfactory result that she could see 6/6 unaided right and left (not improved by glasses), and she could also see N.5 right and left at 20 cm. without a reading addition. Retinoscopy suggested that the usual (about −2 D.C. axis 180) amount of residual astigmatism was present in each eye, but her vision was not helped by any correction. Although the pupil diameters were not particularly small, both eyes contained a dense grey capsule with circular apertures 1 mm. in diameter centrally. It seemed to me that this very satisfactory visual performance, without the aid of a spectacle correction, for both distance and near, was possibly due to the juxtaposition of this small stenopæic aperture exactly on the visual axis of the eye, which coincided precisely with the optical axis of the implant.

The above case reminded me of certain patients with bilateral senile cataract whose sight, instead of becoming worse as the cataracts got denser, paradoxically improved. Most ophthalmologists have seen such elderly patients who announce with pride and joy that for the first time for many years they can see to thread a needle without reading glasses; and they can still see very well in the distance, also without glasses. These patients often have well-developed peripheral lens opacities, with a narrow central red-reflex; on slit-lamp microscopy it is sometimes possible to make out that the opacities are mainly posterior cortical, with a small clear space (of 1–2 mm. diameter) in the very centre of the posterior part of the lens.

I thought that if these optical arrangements could be reproduced on the implant itself, it should be possible to repeat the benefits, so reducing considerably both the residual cylindrical correction and the need for a reading addition in cases of aphakia which had been corrected by anterior-chamber implants.

I therefore designed a modified implant. A circular disc, 6 mm. in diameter, and 0·1 mm. thick, composed of black 'Perspex' (Choyce 1960b), and with a central aperture of 1 mm. diameter, is thermally fused to the posterior surface of the optic of a standard implant, which already carries a suitable correction for the individual patient. This implant, and its position in the eye, is shown in the figure.



The implant with built-in stenopæic aperture (above), and its position in the eye (right).

Although this device is shown incorporated in a standard Choyce anterior-chamber implant, it could also be fitted to the optic portion of any posterior or anterior chamber lens used to correct aphakia, provided the implant is made from perspex.

Clinical Experiences

For straightforward cases of aphakia in patients of presbyopic age, I am on the whole quite satisfied with the results achieved with my standard anterior-chamber implant, and there would be no purpose in using the new implant for these cases.

To begin with, therefore, I treated three unusual cases of uniocular aphakia in elderly patients; they all had some degree of traumatic mydriasis (so that their smallest pupil diameter in bright light was not less than 4 mm.) and also early senile degenerative changes at the macula. Their best visual acuity with aphakic correction was 6/24, 6/18, and 6/12. If they had been fitted with standard implants their visual acuity would have been no better, and they would probably have complained of some photophobia because of the continued mydriasis. When these new implants with a built-in stenopæic aperture had been inserted, their unaided visual acuities were 6/18, 6/12, and 6/9.

Because retinoscopy is unsatisfactory through a 1 mm. aperture, I had to rely on subjective tests for the post-operative refraction of these patients. This was:

Case 1: $\frac{+4{\cdot}50 \text{ D.S.}}{-0{\cdot}75 \text{ D.C. axis } 180^\circ}$ = 6/12 and N.10

Case 2: $\frac{+5{\cdot}00 \text{ D.S.}}{0}$ = 6/9 and N.8

Case 3: $\frac{+2{\cdot}50 \text{ D.S.}}{-0{\cdot}50 \text{ D.C. axis } 180^\circ}$ = 6/6 and N.6

No reading addition was required in any case, and the residual cylindrical error had been substantially reduced. The average of +4 D.S. still required for distance and near vision was probably due to the heat and pressure needed to fuse the black wafer to the posterior surface of the optic, which had flattened this surface to some extent, thus reducing its dioptric power.

* This implant was first described at the annual congress of the Ophthalmological Society of South Africa, in Cape Town, on Sept. 25, 1961.

An allowance was made for this factor and two further cases were treated:

Case 4: $\frac{-1{\cdot}50 \text{ D.S.}}{0} = 6/9$ and N.8.

Case 5: $\frac{-1{\cdot}00 \text{ D.S.}}{-2{\cdot}00 \text{ D.C. axis } 180^\circ} = 6/6$ and N.5.

No reading addition was required in either.

The slight spherical over-correction evident in these two cases was put right in the next three patients to be treated. In all three the unaided vision is 6/9+ and N.6, and therefore spectacles are not needed since their operations.

Muscle balance in four cases was within normal limits, but one case had a manifest left divergent squint.

Macular stereopsis (the Wirt stereotest) was: case 1, not elicited; case 2, 50%; case 3, 90%; case 4, not elicited (divergent squint); and case 5, 95%.

Residual aniseikonia, as measured with AO space eikonometer, was not elicited in cases 1 and 4, and was 0% in cases 2, 3, and 5.

The *peripheral fields* in all five cases were full to a 5 mm. white test object at 330 mm.

Scotopic vision has not been tested objectively, but the patients have not noticed any difficulty in seeing in twilight with the operated eye.

Advantages

As judged by this small series, the advantages of providing an implant with a built-in stenopæic aperture appear to be:

More rapid recovery of visual acuity after operation.

Better unaided visual acuity.

Increased depth of focus, as shown by the fact that the best reading performance is with a distance correction, and no additional correction is required for reading.

Considerable reduction in the residual cylindrical correction (−0·65 D.C. axis 180, compared with −1·92 D.C. axis within 30° of the horizontal in the average thin-implant case).

Elimination of the residual aniseikonia resulting from uniocular aphakia.

Photophobia is not present where it would otherwise be experienced because of moderate traumatic mydriasis.

The above advantages have been gained without sacrificing the peripheral field or the ability to see under conditions of low illumination.

Disadvantages

The surgeon must be sufficiently sure of his technique to guarantee that the implant will be properly centred with the stenopæic aperture lying on the visual axis of the eye. Even 2 or 3 mm. out would certainly detract from the visual result.

Ophthalmoscopy is difficult through this 1 mm. aperture. I think I could diagnose a fairly obvious lesion—e.g., optic atrophy, thrombosis of the central retinal vein, or a retinal detachment—but if more detailed examination of the fundus became essential, as for the localisation of retinal tears in a retinal detachment, further steps might have to be taken. If the pupil becomes dilated to 7 or 8 mm. with mydriatic drops, that should suffice, because there would then be a gap between pupil margin and black optic through which the fundus could be studied. If it did not dilate widely it might be necessary to replace the implant with a standard (wholly transparent) implant or to remove it and not replace it.

Uses of this Implant

The five cases summarised above are satisfactory, and therefore this implant may be of use in similar cases—i.e., of uniocular aphakia in elderly patients with some degree of traumatic mydriasis and with or without degenerative macular lesions.

The implant may also be of use in younger patients—i.e., those well below the age of presbyopia. At present young patients whose uniocular aphakia has been corrected by a standard implant usually need a correction for distance as well as for near vision, and many of them have been supplied with a bifocal lens for their operated eye. It would clearly be an advantage if these patients could be provided with an implant which obviates the necessity for a reading addition, and I plan to treat a few such cases with this new implant in the immediate future.

Conclusions

On theoretical grounds, correcting aphakia by means of an intraocular lens with a stenopæic aperture, of 1 mm. diameter, posteriorly and very close to the nodal point of the eye, should result in optimum vision, both distant and near, without any residual spherocylindrical spectacle correction.

Such an implant has been designed; and, when used for five aphakic patients, it has in fact fulfilled these requirements. If these early results are confirmed, a two-stage technique will be available which can restore optimum unaided distant and near vision to patients with cataract.

The procedure comprises cataract extraction with iridectomy, followed after 6–8 weeks by insertion of a suitable anterior-chamber implant, with a built-in stenopæic aperture. This may be achieved without sacrificing the peripheral field or scotopic vision, but the implant interferes to some extent with the ophthalmoscopic examination of operated cases.

I am grateful to Mr. P. M. Caudell, of Rayners, Ltd., 100, New Bond Street, London, W.1, for overcoming so quickly the technical difficulties involved in making these new implants.

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EMERGENCY ANÆSTHESIA APPARATUS

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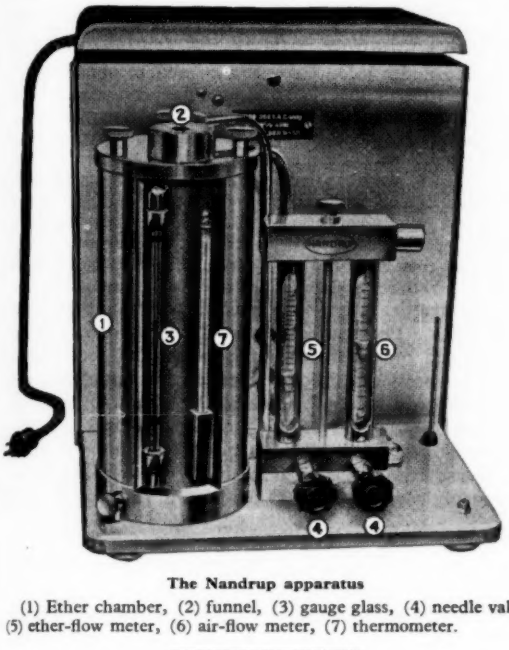
THE growing interest in emergency equipment for anæsthesia has underlined the need for a simple apparatus that does not depend on steel containers holding oxygen and nitrous oxide (Hjorth et al. 1957). This problem has been approached by means of apparatus for anæsthesia by inhalation which make use of liquid anæsthetics and take oxygen from the atmospheric air.

Two types are available; in both, atmospheric air is used partly for ventilation and partly as a vehicle for a volatile anæsthetic. The two types are the E.M.O. or Oxford vaporiser (Epstein and Macintosh 1956) and the Nandrup apparatus (Nandrup 1957a, 1957b, 1958). The E.M.O. vaporiser has the advantage that it is independent of other sources of power than the anæsthetist or the patient, according to whether respiration is controlled or spontaneous. The Nandrup apparatus, on the other hand, normally depends on electric current; but this is unimportant since it is difficult to imagine a serious operation without electric lighting, which means that the necessary electricity can be taken from the emergency lighting plant. Moreover, the Nandrup apparatus can function without electricity as the source of power. Unlike the E.M.O. vaporiser, the Nandrup apparatus indicates on flow-meters, in connection with a non-rebreathing technique, the extent of ventilation—i.e., the alveolar ventilation is known throughout the period of anæsthesia—so this apparatus comes closer to the " conventional " hospital equipment.

I describe here experience with the Nandrup apparatus.



The Nandrup apparatus

(1) Ether chamber, (2) funnel, (3) gauge glass, (4) needle valve, (5) ether-flow meter, (6) air-flow meter, (7) thermometer.

The Apparatus

The Nandrup apparatus weighs 16·2 kg., and its exterior dimensions are 38 × 30 × 28 cm. It permits the administration of accurately measured, low concentrations of volatile anæsthetics. Although mainly intended for ether it can also be used for, say, trichloroethylene, vinyl ether, or halothane. (As far as I know, previous publications have dealt with the use of this apparatus for ether analgesia only.)

The apparatus consists of an electromagnetic, sparkless compressor, which pumps two streams of atmospheric air to a respiration bag, partly via a flow-meter adjusted for atmospheric air, with divisions from 0 to 15 litres per minute, and partly via a vaporiser (the temperature of which is constant, being independent of the surrounding temperature) with flow-meter adjusted for a mixture of air and ether in such a way that direct readings can be taken of the quantity of pure ether used per minute. When other liquid anæsthetics are used, a flow-meter scale for the agent in question replaces the ether scale.

Normally the apparatus is driven by 220-volt alternating current, but it can also operate on an accumulator or on any emergency lighting plant. In the event of no electricity whatever being available, it can be driven by a hand- or foot-operated compressor.

Ether Analgesia

The apparatus was tested clinically with an ether-air mixture in the analgetic dose specified by Nandrup, which is based principally on the analgesic states controlled electroencephalographically (Artusio 1955).

Of 50 patients, aged 16–81 years, selected at random, 41 underwent intra-abdominal surgery, while the remaining 9 were operated for extra-abdominal complaints. The patients were pretreated 1–2 hours before operation with phenobarbitone sodium 100–300 mg. and atropine sulphate 0·3–0·8 mg.; but 4 patients received atropine and pethidine, and, owing to an oversight, 1 had no premedication. The duration of the operations varied from 20 minutes to 3 hours 25 minutes.

In all cases anæsthesia was induced by thiopentone sodium intravenously until consciousness was lost, after which succinylcholine iodide (' Curasit '), gallamine iodide (' Relaxan '), or tubocurarine chloride (' Tubocurane ') was administered for intubation; all patients were ventilated with atmospheric air during this treatment. Ether was first added after intubation in order to avoid irritation of the gastric mucous membrane.

Immediately after intubation the patients were ventilated with ether in a concentration of 2·5–3·5% by volume, according to their physical condition, for 10-15 minutes, after which they were stabilised in the analgesic stage until extubation on an ether concentration of about 1·5% by volume, still with controlled respiration and non-rebreathing technique. Muscular relaxation was maintained by means of one of the relaxing agents already mentioned. The flow of ventilation varied from 8 to 12 litres per minute during the operation.

About 10 minutes before anæsthesia was to be terminated, the ventilation was reduced to about 5–7 litres per minute, and this was continued until the patient's respiration was spontaneous. Where relaxan or tubocurane had been used, atropine and neostigmine were now administered in the usual doses.

In order to verify that the patients really were in a stage of analgesia, they were contacted frequently during the operation—for example, by asking them to answer by head movements such questions as " Can you feel any pain ? ", " Are you lying comfortably ? ", " Are you sleepy ? ". Both spontaneous and requested muscular movements by the patients were registered; blood-pressure, pulse, moisture of the skin, &c., were checked frequently. (Generally speaking, the appearance of perspiration was found to be a good indication of too light analgesia and sensation of pain.)

The same stability of blood-pressure and pulse-rate was observed in these patients as in those treated concurrently in the department with general-anæsthesia/analgesia: nitrous oxide and oxygen, relaxation, and controlled respiration. No symptoms of the excitation stage were found when the ether concentration was increased experimentally in a few patients; nor was there any reflex irritability in the superficial planes of ether anæsthesia, which is contrary to the classical description by Guedel (1937).

The patients awoke without difficulty at the desired time and were able immediately to give adequate replies to simple questions. Postoperatively, the patients were watched in the observation room for a couple of hours. Of the 50 patients, 44 had total amnesia, and 6 had heard voices now and again and had had painless sensations in the abdomen. 3 thought they had dreamed during the operation, but could not remember their dreams.

12 had slight nausea, and, of these, 5 actually vomited. Apart from this, the postoperative period was free from complications. The analgesic condition described by Nandrup, in which the patients should remain for several hours postoperatively, was not ascertained with certainty, possibly on account of the somewhat shorter duration of operation than in Nandrup's series.

The first postoperative specimen of urine of 23 patients selected at random was tested for urobilin, bile pigment, and diastase. A positive urobilin reaction was found in 6 cases. In 4, negative reactions were obtained from the ensuing samples of urine. The remaining 2, who had undergone cholecystectomy, showed positive values for some time postoperatively. Positive urine values are observed for a long time postoperatively in "classical ether anæsthesia; and their low prevalence in the present series may be related to the light dose of ether.

The risk of explosion may be ignored since an ether-air mixture does not become explosive until there is an ether vapour concentration of from 1·85 to 36·5% (Ebersole and Artusio 1957)—that is, a higher concentration than that required for the maintenance of general analgesia.

Trichloroethylene Analgesia

On the hypothesis that all inhalation anæsthetics are equally harmless in weak—that is, analgesic—concentrations, the ether in Nandrup's vaporiser was replaced by trichloro-

ethylene, which was then tested clinically on 50 patients, aged 4–74 years, selected at random. The operations comprised 39 intra-abdominal, 1 intrathoracic, and 10 extrathorax and extra-abdominal operations, with duration of anæsthesia varying from 20 minutes to 4 hours 5 minutes.

Premedication and technique were the same as for ether-air analgesia, except that in these cases, instead of awaiting intubation, the patients were given trichloroethylene immediately after sleep had been induced by means of intravenous thiopentone sodium. A scale can be fixed to the ether flowmeter to permit direct readings of the quantity of pure trichloroethylene used per minute.

According to the patient's physical condition, trichloroethylene 0·7–1·0% by volume was administered initially for 7–10 minutes, and the analgesic stage was maintained by 0·3–0·4% by volume. It was possible to stop administering trichloroethylene for the last 5–15 minutes of the operation. Full amnesia was found in all 50 patients; and possibly lower concentrations could have been used. No operative or postoperative complications that could be ascribed to the anæsthesia were observed. Postoperatively, nausea seemed less pronounced than with air-ether analgesia, and the analgesic effect seemed to continue in the postoperative hours. This estimate is, however, based on subjective statements by the patients.

Halothane Analgesia

Of 40 patients who received halothane in analgesic doses, 32 were pretreated with barbiturate and atropine, and 8 with pethidine and atropine. The ages of the patients, who were selected at random, varied from 17 to 79 years. 26 of the operations were intra-abdominal and 4 intrathoracic; the remaining 10 patients underwent operations on the extremities. The shortest duration of anæsthesia was 15 minutes and the longest 6 hours. Thiopentone sodium was administered intravenously, after which intubation was effected with the help of relaxing drugs. As with trichloroethylene analgesia, halothane was adminstered before intubation. Otherwise, the same technique was used: controlled respiration—non-rebreathing technique—halothane in analgesic doses.

0·5% halothane by volume was found to be the safe maintenance dose for general analgesia. It was used in this way on a 45-year-old woman weighing 111·5 kg., who was operated for a parovarian cyst, and postoperatively she stated that she had felt nothing. The introduction could be made quickly—in less than 2 minutes—or more slowly, as desired, with the percentage of halothane varying from 1·0 to 2·5.

Halothane was found to be very useful, although, as expected, it had a low analgesic range—for instance, it was difficult to contact the patients during the operations. Of the 40 patients, 2 remembered sensation of pain and discomfort, and these had experimentally been given 0·35% halothane by volume as the maintenance dose. Several patients had been in analgesia with total amnesia on 0·4% halothane by volume.

The patients were not very drowsy postoperatively. An initial fall in blood-pressure, accompanied by bradycardia, which is often found in halothane anæsthesia, was not observed, presumably partly because of the short induction with moderate concentration of anæsthetic and partly because sufficient atropine was administered. The effect of the relaxing drugs was not found to be intensified by halothane in analgesic doses.

Halothane Anæsthesia

If relaxing drugs are not to be administered, the Nandrup apparatus can be used for anæsthesia in the "surgical" stage, with the patient breathing spontaneously. Halothane was used in this way as the sole anæsthetic in connection with atmospheric air for 35 patients, selected at random, whose ages varied from just 2 years to 75 years. The non-rebreathing technique was also applied here.

Of the 35 patients 25 were pretreated with barbiturate and atropine and 5 with atropine only. In 26 anæsthesia was induced by means of intravenous thiopentone sodium, while for the remainder halothane was also used to obtain sleep. 13 patients were intubated and 22 were not. The duration of anæsthesia varied from 25 minutes to 3 hours 15 minutes.

10 of the operations were in the abdominal region—for example, herniotomy, appendectomy, and prostatectomy. The remaining 25 were varied—for example, osteosynthesis, arthrotomy, resection of varicose veins of the legs. 7 of the patients were ambulant (i.e., precisely cases for which a portable apparatus is necessary): 2 strabotomies on children, 1 pyorrhœa treatment in a young woman, 2 bloodless repositionings of fractures under X ray, and 2 tonsillectomies.

No difficulties were experienced with air-halothane anæsthesia. The patients went to sleep and awoke quickly, and muscular relaxation was sufficient. There was no cyanosis or clinical evidence of accumulation of carbon dioxide. Approximately the same dosages of halothane were used as in the department's routine halothane/oxygen and nitrous oxide/spontaneous respiration anæsthesia—perhaps 0·25–0·5% by volume more, presumably corresponding to the lacking effect of nitrous oxide.

Discussion

No supplementary analgesics were used in any of the various types of anæsthesia.

Despite its small size, the Nandrup apparatus fulfils all the requirements of a modern anæsthetist. Moreover, it meets the special demand for an instrument that is independent of steel cylinders with compressed gases, which is important since the manufacture or transport of such cylinder may easily be interrupted during civil or military crises (*Lancet* 1959).

The general analgesia and anæsthesia administered with this apparatus appear, judged clinically, to be equally as safe and effective as those obtained with conventional equipment.

The non-rebreathing technique is a condition for the correct application of the apparatus. Here, the Ruben valve has been used (Ruben 1955). This has the advantages that the extent of the ventilation, and thus the alveolar ventilation ensured, is known during the entire anæsthesia, and that it is possible to ensure that the concentration of the anæsthetic administered is that registered on the flow-meters. Problems in connection with the absorption of carbon dioxide are avoided (Dobkin 1958), and, as the patient's expired air does not come into contact with the anæsthesia apparatus, the requirements as to hygiene can easily be met, even under the pressure of treating mass injuries.

The use of atmospheric air partly as a source of oxygen and partly as a vehicle for volatile anæsthetic is a simplification which should not entail any risks. Measurements of carbon dioxide show low values, and the content of oxygen in the arterial blood remains within the normal range (Nandrup 1961). Oxygen saturation and carbon-dioxide tension in the blood do not need to be considered since the important factor is the extent of the ventilation—which is known when non-rebreathing systems are used—and not the concentration of oxygen, provided that this is over 18% (Elam et al. 1958). The vapour concentration necessary for the administration of analgesia or anæsthesia with a Nandrup apparatus causes a negligible fall in the percentage of atmospheric air inhaled (Nandrup 1958).

The use of moist atmospheric air for ventilation will prevent drying of the mucous membrane of the respiratory tract, and it may be assumed that extensive changes

in the physiological equilibrium of gases in the body are avoided (Parkhouse and Simpson 1959).

Summary

The portable Nandrup anæsthesia apparatus has been tested clinically with atmospheric air and volatile anæsthetics. The apparatus functions satisfactorily; and the quality of the anæsthesia, judged clinically, is the same as that obtained with conventional apparatus.

The Nandrup apparatus is suitable not only as emergency equipment but also where general analgesia is required.

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Medical Societies

MANCHESTER MEDICAL SOCIETY

Muscle Disease

AT a meeting of the section of medicine on Oct. 25, Dr. J. N. WALTON discussed Current Concepts of Muscle Disease.

He said that, while a great deal of new information has come to light in recent years concerning diseases of muscle, many problems still require elucidation, and many of the syndromes recently described have brought complexity rather than clarity.

Progressive muscular dystrophy can be defined as genetically determined, primary, degenerative myopathy, and can probably be classified into three main groups which are clinically and genetically distinct. These are the Duchenne type, the limb-girdle type, and the facioscapulohumeral type. The rare ocular and distal types also seem to be definite entities.

Turning to myotonia, Dr. Walton remarked that there is still controversy as to whether myotonia congenita and dystrophia myotonica are separate diseases or variants of a single disease. Many cases previously diagnosed as myotonia paradoxa were probably cases of a congenital phosphorylase deficiency giving rise to a form of glycogen-storage disease of muscles (McArdle's syndrome).

In the diagnosis of muscular dystrophy, electromyography and muscle biopsy are important; but the most sensitive method of early diagnosis is estimation of the serum-aldolase, which is often raised to very high levels before any clinical sign of the disease is apparent.

The nature and pathogenesis of polymyositis still remain obscure. Many patients with this condition show no skin change or constitutional upset; and in the past these would commonly have been regarded as having muscular dystrophy. Differential diagnosis is by no means academic, since the majority of cases of polymyositis respond to steroid therapy. In polymyositis the possibility of associated malignancy must always be borne in mind, particularly in cases with severe skin changes. Muscle biopsy is valuable in diagnosis; but the histological changes in certain subacute forms of polymyositis, and in some of the more rapidly progressive varieties of muscular dystrophy, show a considerable degree of overlap; and diagnosis must depend on a combination of clinical, electromyographic, and histological findings.

Reviews of Books

A Short History of Clinical Pathology

W. D. FOSTER, M.D., consultant pathologist, Dudley Road Hospital, Birmingham. Edinburgh: E. & S. Livingstone. 1961. Pp. 153. 27*s*. 6*d*.

IT was brave to write the history of a specialty which some say has yet to be born and which others declare is already showing signs of decay: to have written it so well deserves admiration and gratitude. It is true, of course, that even if in the evolutionary scale of medicine the clinical pathologist is still a young and immature species, clinical pathology certainly is not. Its roots spread widely and deeply into history—too widely and too deeply perhaps ever to produce a single plant. These far-flung origins have made it necessary to divide this book into separate chapters for morbid anatomy and histology, chemical pathology, clinical bacteriology, serology, and hæmatology; and their stories hardly overlap. (Only Ehrlich—and we are unlikely to see his like again—leaves his mark on each.) What does, however, give unity to the book is the even excellence of the writing: its style is simple yet elegant and scholarly.

Taken separately, each chapter contains an abundance of information about the past, and a few teem with morals for the future. The history of bacteriology in particular reads like a cross between a best-seller and an educational tract. How recently was it that practically the whole of the medical establishment of Europe declared themselves neither amused nor convinced by the germ theory (propounded by a band of cranks some of whom were not even medically qualified); and how stubbornly did they cling to their beliefs! How modest and arduous were the beginnings and how breathtaking was the growth of the modern hospital laboratory! Chemical pathology lends itself least readily to the historical treatment: perhaps the strange love affair between biochemistry and clinical medicine which gave it birth still smacks faintly of scandal.

To complement the historical sections, Dr. S. C. Dyke has contributed a valuable chapter on the present-day organisation of clinical pathology. The index, which omits the name of Pasteur, is not entirely satisfactory.

Patients' Views of Medical Practice

ELIOT FREIDSON, New York University and Montefiore Hospital. New York: Russell Sage Foundation. 1961. Pp. 268. $3.75.

THIS is a study, by questionary and interview, of the reactions to medical care supplied to subscribers to a prepaid medical plan in The Bronx, New York. In 1955 the author was appointed social-science resident in the Family Health Maintenance Demonstration—a temporary experimental offshoot of the Montefiore Medical Group. The parent group, itself a part of the Health Insurance Plan for Greater New York, sets out to supply its subscribers not only with the services of a specialist team and the technical resources of a hospital but also with the equivalent of a family doctor in the shape of an " internist " member of the group, the subscriber choosing his internist from several available. The offshoot offered a team—doctor, nurse, and social worker—ready to give a full service on request and even to take the initiative in aftercare or in preventive medicine, with the family, not the single patient, as unit. It is an essential part of the situation that private practitioners, outside the group, were also available; the patients were largely free to choose the kind of medical service they preferred and many had experience of all three.

Mr. Freidson set out to discover what in the way of medical care these people wished for, how they liked what they got, and how they reacted to it. He found they wanted " competence " of the kind supplied most fully by specialists in a well-equipped hospital, but also " personal interest " which many found more or less lacking even in the Montefiore group. They were by no means certain of getting " their own doctor " when they wanted him, and home visits, especially at night, were,

apparently, not easily come by. The Family Health Maintenance team received high praise from many patients, though the social worker was used and appreciated much less than the doctor and nurse; but there was a disconcerting tendency for both group and Family Maintenance patients to " go outside " for operations, confinements, night visits, and " independent opinions ", which they believed they could not get within the group.

Mr. Freidson points out that the population of The Bronx is not typical of the whole country, but his careful and detached observations are illuminating and his cautious opinions well worth attention. An appendix gives the questionaries in full.

In Search of Criminology

LEON RADZINOWICZ, Wolfson professor of criminology and director of the Institute of Criminology at Cambridge University. London: Heinemann. 1961. Pp. 254. 25*s*.

IMPENDING developments in Cambridge criminology led Professor Radzinowicz to examine in detail what was happening in other countries, mainly in Europe and the U.S.A.; and his formidable erudition has turned the book into a history of academic criminology. With a bibliography of some 700 items and extensive annotations, it is a valuable source of reference to landmarks in criminology, but it is not a textbook and it will appeal to a limited number of readers.

Inevitably, one is led to compare the European with the American scene. Radzinowicz's criticisms of the Continental stagnation which has often followed the pioneering " golden age " of criminology are the more effective for the kindly and understanding way they are phrased. The United Kingdom, which lagged badly in academic recognition of the new discipline, now spends more than any other European country on research—£60,000, out of a Continental total of a mere £100,000 or so. But in the U.S.A. there are individual projects which are costing more than twice the whole annual European research budget. In the longest section of the book, Radzinowicz pays tribute to this American work, and he values much of it very highly indeed. The rest of the world, he says, needs to learn from the American example. Sadly, that troubled country needs all the criminology it can get. Radzinowicz's sympathy towards criminologists who started life in criminal law is evident, and the origins of his present department and its orientation are to be found in this book. Transatlantic work is mainly criticised for its sociological origins, and for the neglect of criminology during legal training.

A History of Thoracic Surgery

RICHARD H. MEADE, B.S., M.D. Springfield, Ill.: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1961. Pp. 933. 220*s*.

WHEN the term history is applied to such a young and growing subject as thoracic surgery one may expect to look back into the distant past as well as recall events within living memory. This is what Dr. Meade has done in a comprehensive work containing more than 100 photographs, with short biographies, of surgeons dead and alive who have made important contributions to surgery of the chest.

Inevitably, much of the history is recent and some of those who have contributed to it are fortunately still active, but early attempts and thoughts on the treatment of heart and lung disease are given the special prominence due to men of vision and imagination. In a sense the chapters as they appear are the story of the evolution of a great branch of medicine. Most of the steps forward were logical, but occasionally opportunity and daring made a sudden jump. Unfortunately, in many ways, the historian has to depend on the written word and he has continually to bear in mind that many failures, though brilliant in concept, did not reach publication.

Anyone who has written articles on thoracic surgery knows the problem of getting references for the opening historical paragraph. Far too many variations and inaccuracies have occurred in individual papers, but now there is an almost infallible source based on a long, painstaking, and scholarly study. Dr. Meade is to be congratulated and thanked for what he has done. Many of the classic publications have been freely quoted, and the method of composing each section so that the appropriate highlights are brought out is admirable.

Some omissions were inevitable. For example, though Richard Lower features in connection with blood-transfusion he is not referred to in the chapter on pericarditis. But apart from very minor omissions (and an occasional error in the spelling of proper names) there can be little but praise for the style and presentation. It is intriguing to read of the isolated ventures of the giants of the past, and to realise that suddenly, after a long interval, there was a break and the whole subject became a practical proposition, with a mass of modifications and improvements within a few months of the original success.

This book gives the full story of the background and development of this specialty. All thoracic surgeons should read it, and many physicians as well as surgeons will find it fascinating and informative. This young and exciting subject deserves the historian that it has acquired in Dr. Meade.

Gynæcology for Students

LANCE TOWNSEND, M.D., F.R.C.S.E., F.R.A.C.S., F.R.C.O.G., professor of obstetrics and gynæcology, University of Melbourne. Melbourne: Melbourne University Press. London: Cambridge University Press. 1961. Pp. 325. 63*s*.

FOR several decades it has been customary in the University of Melbourne to supply undergraduates with printed notes on gynæcology. These notes have recently been revised by Professor Townsend and illustrations added to produce this book. With one or two minor exceptions, the teaching of the Melbourne school follows closely the practice of gynæcology in this country. The material is carefully chosen and clearly presented, and there are many excellent illustrations and drawings. The sections on malignant disease of the genital tract and on diseases of the ovary are very effective, and the main steps of the common gynæcological operations are described briefly in the last chapter.

The presentation is largely didactic and this may sometimes be an advantage, but there are chapters where it is an obvious weakness. For example, the section on infertility contains lists of ætiological factors and possible lines of investigation and treatment, but there is little or no discussion of the wider issue or of the emotional difficulties that may be associated with childlessness. With the present curriculum and examination system, however, students will find this a useful book.

The Making of a Surgeon

IAN AIRD, CH.M., F.R.C.S. London: Butterworths. 1961. Pp. 140. 12*s*. 6*d*.

OVER the past twenty-five years or so, Professor Aird has been concerned with the training of many thousands of postgraduate students from all parts of the world. His writings and his travels have influenced the education of very many more. For those who are contemplating, or are already embarked on, a surgical career he has now set down an account of the qualifications they must obtain, and the abilities they must acquire or cultivate. He deals comprehensively with the successive phases in a surgeon's progress, from his last years at school to the time when, as a consultant, he assumes complete responsibility for his patients. There are further chapters on different specialties, and on the pattern of surgical training in twenty foreign and Commonwealth countries.

Some of the topics are treated impersonally: most are seen in the light of Professor Aird's experiences, and many are enlivened with episodes from his reminiscences. His book is of most interest to the youngest members of the profession, but their seniors should not discount it. Unsuccessful applicants for a consultant post may not enjoy discovering which aspects of their training were at fault: but they will be encouraged to know that this distinguished author was himself, over a period of ten years, turned down for a succession of ten appointments to which he aspired.

THE LANCET
LONDON 2 DECEMBER 1961

Pharyngitis and Rheumatic Fever

TEN years ago a series of important studies on streptococcal sore throat was begun in the U.S.A. at the Warren Air Force Base. One of the most significant findings was that sore throat associated with group-A streptococci was followed by acute rheumatism in about 3% of cases.[1] Subsequent investigation showed that chemotherapy could greatly reduce this risk.[2] Largely because of the findings at Fort Warren, the Committee on Prevention of Rheumatic Fever [3] recommended that all patients with streptococcal pharyngitis should be given a ten-day course of penicillin in order to prevent rheumatic fever. This recommendation has not been generally applied to civilian communities for two reasons: firstly, many workers have found that acute streptococcal and non-streptococcal sore throat are clinically indistinguishable [4–8] so that, in the absence of bacteriological control, all cases of sore throat would have to be treated; and secondly, evidence [9 10] from the United States suggests that outside special environments, such as that at Fort Warren, the incidence of acute rheumatism following bacteriologically proven sore throat is very much lower than 3%. Investigations in this country involving closed populations at a Dr. Barnardo's Home [11] and at a military camp [7 8] have also pointed to the benign nature of streptococcal sore throat. A study by SIEGEL et al.[12] of 2545 children with sore throat who attended a pædiatric clinic in Chicago supplies further evidence that untreated endemic pharyngitis carries only a small risk of rheumatic fever. β-hæmolytic streptococci were isolated from 1213 (48%) of the children, and of these streptococci 86% were of group A. Patients with streptococcal infection were divided into two groups, of which one was treated with a single intramuscular injection of 600,000 units of benzathine penicillin, while the other received no chemotherapy. Among the 605 treated children no case of rheumatic fever was found. Of the 608 control patients 2 (0·3%) developed rheumatic fever.

When the risk of rheumatic fever following streptococcal sore throat is high, as it was at Fort Warren, prophylactic chemotherapy may be justified; but where this risk is slight the gain in protection may be outweighed by the hazard of sensitisation to penicillin.[13 14] Can we, then, recognise circumstances in which the incidence of rheumatic fever following streptococcal sore throat will be predictably high? Earlier work established that epidemic sore throat may be associated with an unusually high risk of rheumatic fever,[15 16] that there is a genetic predisposition to this disease,[17 18] and that patients who have had a previous attack are especially susceptible to further attacks.[19] Moreover, streptococci differ in pathogenicity—this is exemplified by the preponderance of type-12 streptococci among nephritogenic strains.[20] Possibly the differences in incidence of rheumatic fever between more or less similar populations—for instance, military recruits [1 8]—are due at least partly to differences in the infecting organism. The properties of the organism that are likely to be most important in this respect are "communicability" [21] and virulence. Unfortunately, these terms are used by different workers in different senses. Certain types of streptococci undoubtedly spread freely in the population, whereas others do not; but to what extent this depends on properties of the organism or of the population, or of both together, is undecided. Virulence of streptococci could be defined in terms of ability to produce severe sore throat, stimulation of antibody production, persistence of the streptococcal carrier state, or production of rheumatic fever. Evidence from the Chicago study [12] supports previous findings that rheumatic fever is most likely to follow sore throat which has been clinically severe with high fever and a high white-blood-cell count. The relation of antibody production to rheumatic fever is fairly clear. When rheumatic fever follows streptococcal infection the antistreptolysin-0 titre usually rises to a high level [22]; but this high titre is associated with the appearance of the rheumatic process, and estimation of the titre at the onset of the sore throat is no guide to the subsequent risk of rheumatic fever. Penicillin administered early in the infection eliminates the streptococcus and thereby suppresses not only the rise in antistreptolysin titre but also that of type-specific antibody.[23] The Chicago workers [24] suggest that this may be a further reason for withholding routine chemotherapy in endemic streptococcal sore throat since the antibody, once produced, persists [25] and may protect against reinfection by the same streptococcal type.

With growing evidence that rheumatic fever only occasionally follows streptococcal sore throat, there

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20. Rammelkamp, C. H., Jr., Weaver, R. S. *J. clin. Invest.* 1953, **32**, 345.
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22. See *Lancet*, 1960, ii, 479.
23. Breese, B. B., Disney, F. A., Talpey, W. B. *J. Dis. Child.* 1960, **100**, 353.
24. Siegel, A. C., Johnson, E. E., Stollerman, G. H. *New Engl. J. Med.* 1961, **265**, 566.
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seems at present to be no justification for aiming at the prevention of rheumatic fever by routine chemotherapy in all cases of acute sore throat. On the other hand, it is essential to eliminate streptococci from the throats of patients with severe bacteriologically proven streptococcal sore throat, with epidemic streptococcal sore throat, with a convincing family history of rheumatic fever, or with a previous history of acute rheumatism.[26] For prophylaxis a four-to-five-day course of penicillin (which is often given) is inadequate [7]; an effective blood-level of penicillin should be maintained for ten days.[2]

Steroid Fever

THE mechanism by which fever is produced is ill defined. There is a good deal of evidence suggesting that the fever accompanying infections or sensitivity reactions may be due wholly or partly to release of a pyrogenic substance from leucocytes,[27] but the nature of this substance and its mode of action are unknown. This may not be the only mechanism, since KAPPAS et al.[28] found that intramuscular or intravenous injection of the purified steroid, ætiocholanolone, can cause fever in man, and there is some evidence that this substance may occasionally play a part in naturally occurring fever.

KAPPAS et al.[29] have found that only the 5 β steroid compounds—the ætiocholanolone or pregnane derivatives—are pyrogenic. Such compounds are formed normally during the degradation of adrenocortical and sex hormones, and they are rapidly conjugated and excreted. Conjugation probably abolishes their pyrogenic properties, since ætiocholanolone esters are not pyrogenic [29]: similarly, pregnanolone is pyrogenic, but not its esters. Intramuscular injection of 0·2–1·0 mg. of the free steroids per kg. body-weight causes fever after an interval of 4–8 hours. Slow intravenous infusion of the same dose is followed by a similar delay before the onset of fever, while rapid intravenous injection commonly does not cause fever.[29] The fever can be prevented or diminished by cortisone or salicylates. The compounds are unlikely to be metabolised in any way other than by conjugation, since their conjugates can be recovered almost quantitatively from the urine.[30]

That the free steroids cause fever directly seems improbable because their half-life after intravenous injection in man is less than 1 hour, and the unconjugated steroid cannot be detected in plasma during the latent period between injection and onset of fever. Possibly unconjugated steroid is concentrated in certain tissues, despite its absence from blood: there is no direct evidence of this, but unconjugated œstradiol has been shown to be concentrated in the uterus after intravenous injection,[31] and unconjugated 5 β steroids may behave similarly. No pyrogen has been detected in plasma taken at the height of the fever [32]; but, though circulating pyrogens have been demonstrated in animals with infection, their detection in febrile patients has proved much more difficult,[33] and failure to detect a circulating pyrogen during steroid fever does not necessarily denote its absence. The steroids may perhaps cause fever through an inflammatory response at the injection site; local tenderness and swelling, or phlebitis, commonly follow injection. But this explanation is not wholly satisfactory, because many species of animals did not develop any fever after intramuscular, intravenous, or intrathecal injections of the same compounds in doses of 1·0–5·0 mg. per kg.[34]—though it is not clear whether the animals had local inflammatory changes similar to those in man.

These observations may have a bearing on one type of "periodic fever". This term covers at least two distinct conditions. One of these—familial Mediterranean fever [35]—is a familial condition affecting persons of Mediterranean extraction, and beginning in childhood. The attacks of fever are accompanied by abdominal pain, and come on at irregular intervals. Renal failure due to amyloidosis very often causes death. The febrile attacks are unaffected by salicylates and cortisone, but attacks may be preventable by a low-fat diet.[36] In this condition, BONDY and his colleagues have found no evidence of abnormal steroid metabolism.[37]

A second type of periodic fever has been described by BONDY et al.[37] The patients all had raised levels of free ætiocholanolone in the plasma during their attacks of fever, but not during remissions (in other patients with fever due to infective or inflammatory illness these levels were normal). Clinically, these cases differed from those of familial Mediterranean fever in several respects: the patients were of no distinct racial group, fever came on at fairly regular intervals, and the attacks were prevented or relieved by cortisone. Amyloidosis was not found. The condition has been called ætiocholanolone fever.[38] One patient with this disorder was given large doses of testosterone and 11-deoxycortisone, which are metabolised to ætiocholanolone.[38] This did not precipitate an attack, and there was no increase in free plasma ætiocholanolone. Thereafter, he was given a slow intravenous infusion of 11-ketopregnanolone, one of the pyrogenic steroids described by KAPPAS et al.[29]; this compound is not metabolised to ætiocholanolone. 5 hours after the end of the infusion he developed an "impressive" fever, associated with a considerable increase in free ætiocholanolone in the plasma. Patients of this type may possibly respond to any fever with an increase in free ætiocholanolone.

Thus injections of ætiocholanolone and related steroids can cause fever in man, and free ætiocholanolone has been found in the plasma of patients with a fairly clearly defined intermittent febrile disease. An assumption that these findings are related seems reasonable;

26. See *Lancet*, 1960, i, 967.
27. Atkins, E. *Physiol. Rev.* 1960, **40**, 580.
28. Kappas, A., Hellman, L., Fukushima, D. K., Gallagher, T. F. *J. clin. Endocrin.* 1956, **16**, 948.
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31. Jensen, E. V. First International Congress of Endocrinology; Advance Abstracts; p. 733. Copenhagen, 1960.
32. Kappas, A., Glickman, P. B., Palmer, R. H. *Trans. Ass. Amer. Phycns*, 1960, **73**, 176.
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36. Mellinkoff, S. M., Schwabe, A. E., Lawrence, J. S. *Trans. Ass. Amer. Phycns*, 1960, **73**, 197.
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but raised levels of unconjugated ætiocholanolone have been found in a few patients with cirrhosis, some of whom were afebrile.[39] Steroid compounds are unlikely to be commonly concerned in the fever of disease, but they may well play a part in the control of normal temperature and particularly in the production of temperature changes during the menstrual cycle, since the principal metabolites of progesterone are potentially pyrogenic.

Annotations

BACK TO MACKENZIE

BORN in 1853, Sir James Mackenzie is seldom in the minds of the younger generation; but in the Mackenzie lecture to the College of General Practitioners last Saturday Dr. Annis Gillie showed that much of his thought remains as valid as his clinical observations. The boy who left school (with relief) at 15, and made a slow and uncertain start in medicine, proved to be so naturally an investigator that he would have found subjects of investigation wherever he worked. But almost the whole of his research on the failing circulation and on referred pain was in fact carried out in his twenty-eight years of general practice in Burnley; and it was the study of patients over long periods—possible in general practice but so difficult elsewhere—that was particularly characteristic of his method. The man who devised the polygraph and enjoyed accumulating records and tracings was very careful to keep machines in their place: he was even afraid lest his achievements in one specialty should make people pay less attention to his belief that it is the whole body—the interaction of structure and function—that matters. A fuller understanding of early symptoms and their significance for the patient's future were what chiefly attracted him—the knowledge obtainable only by watching how people "withstand the storm and stress of life". His strength as a scientist, Dr. Gillie thinks, lay very largely in his impatience with other kinds of knowledge—the impatience with dogmatic teaching that had made school so boring to him. As Sir John Parkinson has put it, "Mackenzie was not interested much in what was known, but in what was lacking in the understanding of a subject, or of a patient". He distrusted the sort of faith that consists in accepting information because it is taught by tradition. "Your faith in hypod. inj. of strych," he told Dr. Guthrie, "is quite as superstitious as the old woman believing in a personal devil."

Today, said Dr. Gillie, Mackenzie might put out a warning that postgraduate study is not an end in itself but only a means of stimulating the inquiring and critical mind of the true postgraduate student.

GIFTED SCHIZOPHRENICS

LIKE the artist, the schizophrenic sees the world differently from other men; for him it often has a personal or threatening implication—but above all it is full of the unexpected. Speaking at the annual meeting of the Mental Health Research Fund in London on Nov. 20, Prof. G. M. Carstairs remarked that in everyday life we tend to surround ourselves with familiar things, and familiarity dulls perception. This was noticeable on arrival in a foreign country—the sights and sounds were more vividly registered at first than they would be after a few days. The artist and the schizophrenic in their different ways seemed to preserve that acuteness of perception which Sir Herbert Read had described as "the innocent eye"; but the schizophrenic's awareness was not just the freshness of a child's outlook on the world. It was a heightened awareness indeed, but often an awareness heightened by dread.

This illness could sometimes arouse an intense, though usually rather sinister, appreciation of the mystery behind normal phenomena. Earlier in the present century painters of the surrealist school—men such as Dali, Magritte, and Max Ernst—were frankly envious of the schizophrenic's faculty of living in a dreamlike state, even though the dream should often prove a nightmare. In the early 1920s the term "paranoid" had a positive value in æsthetic parlance, and surrealists made it their aim to paint frankly psychotic imagery. This was their tribute to the "magical" quality of schizophrenic fantasy—a quality which was attributed to the unconscious mind.

It was true, of course, that too much deliberation, too much conscious planning and control, could stifle the creative artistic impulse. This was evident in the change which came over children's paintings at about the age of eight: from being lively, spontaneous, and charged with feeling, the child's work all too often became stilted and formal, conforming to his idea of how other people expected things to appear. In the early stages of schizophrenia, feeling his touch with reality to be fading, the patient might try to regain "control" by a return to obsessional mechanisms, which might feature in his painting. In chronic schizophrenia, however, we could sometimes see the undoing of inhibitions which stifled spontaneous creativity, and patients who had never shown any particular aptitude with pencil or brush might produce works of singular naïvety and charm. In these "primitive" works, it was as if the "innocent eye" of childhood had been recovered.

CONTROL OF CELL METABOLISM

ALL living systems require an external source of energy not only for growth and activity but also for continued existence. Organisms capable of photosynthesis (autotrophs) obtain their energy directly from the sun; but in all other organisms (heterotrophs) energy is derived from chemical reactions. Although these energy-giving reactions are numerous, they all have one thing in common: all are coupled to the formation of "energy-rich phosphate bonds". It is the free energy of hydrolysis of these bonds that supplies the energy for all biological activities.

In mammalian cells the two principle bond-producing systems are glycolysis and respiration. In the former system glycogen or certain hexoses are converted to lactic acid. Each hexose moiety gives rise to two molecules of lactic acid, and at the same time phosphate radicals are bound to two or three molecules of adenosine diphosphate (A.D.P.) to form adenosine triphosphate (A.T.P.). The respiratory system then oxidises the lactic acid to carbon dioxide and water, and at the same time 36 molecules of A.D.P. are converted to A.T.P. for each pair of lactic-acid molecules oxidised. Thus the conversion of one unit of hexose to lactic acid is associated with the formation of 2 or 3 energy-rich phosphate bonds, while the complete oxidation of the lactic acid gives rise to a further 36 bonds;

39. Tisdale, W. A., Klatzkin, G. *Yale J. Biol. Med.* 1960, **33**, 94.

so respiration is twelve to eighteen times as efficient as glycolysis in the utilisation of sugars.

Although this outline of glycolysis and respiration suggests that they take place sequentially they usually appear to act in parallel and in competition with one another. This is partly because of differences in the location of the two sets of enzymes which carry out these reactions (the respiratory apparatus is located solely in the mitochondria, whereas glycolysis takes place in the cytoplasm also), and partly because of competition between the two systems for phosphate, A.D.P., and other factors. If adequate amounts of these substances were available the cell would produce lactic acid much faster than the respiratory system could oxidise it. In fact, these factors are present in limited amounts, and since the respiratory enzymes have a greater affinity for A.D.P. than have those enzymes involved in glycolysis there is usually no net production of lactic acid except when, owing to deficiency of oxygen, the respiratory apparatus is not functioning fully.

The converse state—inhibition of lactic-acid formation by oxygen—is known as the Pasteur effect. In some cells (leucocytes and cells of the retina, testis, and most neoplasms) the respiratory system appears to be inadequate completely to suppress lactic-acid formation. Nevertheless, even in these tissues lactic-acid production in the presence of oxygen is considerably less than in its absence. Thus in all tissues respiration suppresses lactic-acid production.

In 1929 Crabtree [1] described the suppression of tissue respiration by glucose in malignant cells. Later this effect was found in normal cells as well. Ten years ago, when the polarographic technique was applied to the problem, the inhibition of respiration was found to be preceded by a brief period of greatly increased oxygen consumption. This seems clearly to be due to the rapid phosphorylation of the glucose by A.T.P. under the influence of hexokinase, which yields an equivalent amount of A.D.P., the deficiency of which limits tissue respiration. The succeeding phase of inhibited respiration, which lasts only so long as any of the added glucose remains, cannot be explained so simply.

Reviewing all this work, Ibsen [2] points to the conflict both in experimental results and in theories. As regards the experimental results the type of buffer in which the tissue is suspended seems to influence the effect of adding glucose. From observation it may reasonably be concluded that pH change is involved in the mechanism; and this supposition is supported by the well-known fact that a fall in pH such as occurs when lactic acid accumulates does diminish the respiration-rate of tissue.

Clinically, the importance of these findings is twofold. First, fuller comprehension of cellular control of metabolism is essential to a proper understanding of the working of the body.[3] Secondly, these findings have a more immediate relevance to the question of lack of oxygen in the tissues due to cardiac or pulmonary insufficiency. When the tension of oxygen in the tissues falls below the "critical oxygen tension", respiration diminishes and lactic acid is formed. This by itself further reduces the respiration-rate. Production of the same number of energy-rich-phosphate bonds from glycolysis as from the oxidation of the substrate by one molecule of oxygen results in the formation of four or six molecules of lactic acid. The cardiopulmonary system can readily remove carbon dioxide from the body; but lactic acid cannot be so eliminated, so the blood-lactate rises. This leads to a fall in pH which can be corrected by the addition of sodium bicarbonate; but the change in pH is only one manifestation of the prevailing tissue hypoxia, for which there is only one remedy—the provision of enough oxygen in the tissues.

1. Crabtree, H. G. *Biochem. J.* 1929, **23**, 536.
2. Ibsen, K. H. *Cancer Res.* 1961, **21**, 829.
3. Regulation of Cell Metabolism: Ciba Foundation Symposium (edited by G. E. W. Wolstenholme and C. M. O'Connor). London, 1959.

INFECTIVE PNEUMOCONIOSIS

WITH about 3500 new cases certified each year, pneumoconiosis in coalminers is Britain's most serious industrial disease. Yet little of the disability or mortality of those affected can be attributed directly to the inhaled dust; most is due to development of the complication known as progressive massive fibrosis (P.M.F.). The proportion of pneumoconiotics in whom P.M.F. develops varies considerably between different areas but may reach 50%.[1] Radiologically, a large opacity appears in a lung field where formerly only the numerous small dust foci characteristic of simple pneumoconiosis were evident.

P.M.F. is widely regarded as an infective pneumoconiosis caused by a combination of tuberculosis and an otherwise relatively benign dust. Certainly tuberculosis can often be demonstrated post mortem (it was present in 75% of Rogers' [2] cases), and lesions very similar to P.M.F. have been produced experimentally by the synergic action of coalmine dust and tubercle bacilli.[3] Nevertheless, only about 2% of patients with P.M.F. have positive sputum during life—suggesting that tuberculosis present at death is a terminal complication. Moreover, chemotherapy has not prevented the usual progression of the disease.[4] The lesions could, of course, be initiated by an infection which then dies out and subsequently be self-perpetuating, but if this is so there are no obvious grounds for incriminating tuberculosis.

It has been apparent for some time that pneumoconiosis predisposes to infection by the group of organisms known as the anonymous mycobacteria. These are probably free-living bacteria which can establish an infection only in especially susceptible people. Experimentally their pathogenicity appears to be enhanced by the presence of coalmine dust.[5] Marks [6] has now recorded the isolation of anonymous mycobacteria from 2% of the men attending pneumoconiosis medical panels in South Wales. He suggests that transient infections may be quite common in men with pneumoconiosis, and that these organisms are as likely as the tubercle bacillus to be concerned in the origin of P.M.F.

Many physicians in this country have been uncertain how seriously to regard frank infections by anonymous mycobacteria, particularly those associated with pneumoconiosis where the question of compensation arises. Kamat et al.[7] have made a clinical study which provides an answer to this question. These workers compared 57 cases of infection with such bacteria in men, including 27 associated with pneumoconiosis, with 57 cases of tuberculosis in men. Hæmoptysis and cavitation were commoner in the "anonymous" infections, especially in the

1. Cochrane, A. L., Cox, J. G., Jarman, T. F. *Brit. med. J.* 1952, ii, 843.
2. Rogers, E. *Lancet*, 1946, i, 462.
3. Zaidi, S. H., Harrison, C. V., King, E. J., Mitchison, D. A. *Brit. J. exp. Path.* 1955, **36**, 539, 545, 553.
4. Miall, W. E., Oldham, P. D., Cochrane, A. L. *Brit. J. industr. Med.* 1954, **11**, 186.
5. Byers, P. D., King, E. J. *J. Path. Bact.* 1961, **81**, 123.
6. Marks, J. *Brit. med. J.* Nov 18, 1961, p. 1332.
7. Kamat, S. R., Rossiter, C. E., Gilson, J. C. *Thorax*, 1961, **16**, 297.

presence of pneumoconiosis. The bacteriological-conversion and mortality-rates were as follows:

	No. of patients	Converted to negative	Not converted	Died
"Anonymous" infections:				
With pneumoconiosis ..	27	6	21	8
Without pneumoconiosis ..	30	20	10	5
Tuberculosis:				
With pneumoconiosis ..	10	6	4	4
Without pneumoconiosis ..	47	37	10	5

These observations establish the gravity of infection with anonymous mycobacteria, especially in pneumoconiosis, and show the need for compensation in cases connected with dust exposure in the same manner as tuberculosis. The relatively unfavourable prognosis is no doubt due to the resistance of the bacteria to most chemotherapeutic agents.

Whatever the genesis of P.M.F., tuberculosis remains an important hazard; and now that other sources of infection have become fewer, the regular bacteriological supervision of patients with pneumoconiosis seems especially desirable from the public-health point of view as well as in their own interest.

MECHANISMS OF MEMORY

THE brain of a simple invertebrate creature like the octopus might seem an uncertain starting-point for a study of human learning and memory; but, as Prof. J. Z. Young pointed out in the 36th Maudsley lecture of the Royal Medico-Psychological Association on Nov. 15, Henry Maudsley had been one of the first to draw analogies between machines and the brain, and to suggest that understanding might come from comparative neurology, starting at the simplest levels. The octopus brain was almost wholly unknown before Professor Young's work, and the journey of exploration had been an exciting experience: it might be an illusion, but he felt now that he was really beginning to understand the parts of this simple brain and the way they worked together.

Memory was best considered as a physical system containing a representation of past events in coded form, a concept which must take account of information within the genes; for any organism (including plants), living homœostatically in an environment must involve the capacity to adjust to changing circumstance. Communication of any kind depended upon a pre-arranged code of symbols relevant to the purpose. Whereas speech and writing, for example, called for complex coding, it had been shown by micro-electrode studies that the frog's eye told its brain just five things—a system simpler than we might think. It was Professor Young's hypothesis that the shapes of dendritic trees within the visual system of the octopus corresponded to specific shapes in the environment: the animal could be trained to attack one shape and not another. Tangential stained sections of the optic lobe showed dendrite shapes of either horizontal or vertical type, and studies of electrical activity showed how the shape of the original visual stimulus might lead to electrical discharge in the appropriate cell body of the optic cortex.

That this hypothesis applied more generally had been suggested by micro-electrode studies of the cat, where cortical cells represented oval fields: each column of cells in the cortex represented sight in a certain direction, but each layer took care of different factors, such as illumination. Studies of perception in other animals and in children had shown the special importance of vertical/horizontal distinction; oblique lines at right-angles were far less easy to distinguish.

Explaining how the octopus learned which symbols meant reward and which ones brought pain, Professor Young showed by selective removal of parts of the brain how the learning process could be impaired. The level of motivation was controlled by a balanced system of excitatory and inhibitory mechanisms. The amplifying excitatory system of relatively large cells might perhaps be comparable to parts of the basal system, particularly the hippocampus and amygdala, of the human brain, which are known to be associated with the basic processes of learning and motivation. More speculatively, the inhibitory action of the vertical lobe of the octopus's brain might point to some of the functions of the prefrontal cortex, also rich in small cells.

PRESIDENT OF THE G.M.C.

Sir David Campbell's twelve-year presidency of the General Medical Council, which ended this week, has seen more changes than any corresponding period since the Council's formation in 1854. The Medical Act of 1950 has had far-reaching effects not only on the profession but on the Council itself; and the way in which that body has adapted itself to the new regime has been largely due to Sir David's wise guidance. His imperturbability and balanced judgment have gained him the very real respect of those who served with him; and his natural attributes of leadership, bonhomie, and capacity for warm friendship have made his associates feel that they were valued colleagues in a joint enterprise.

The office of president of the G.M.C. is no sinecure, and those familiar with its duties and responsibilities must marvel at their being fulfilled by one living more than 500 miles from London. There is much work to be done between sessions; yet not once during his years of office have Sir David's colleagues failed to endorse his decisions.

In the last of his presidential addresses to the Council, he could fairly remark:

> "I think it is true to say that the prestige of the General Medical Council never stood higher than it does today. In our relations with the universities and medical schools of the country a new spirit is abroad. They have found the Council's Recommendations on the curriculum a 'stimulus and a challenge' and have applied themselves with vigour to a comprehensive review of their systems of medical training."

To those outside the Council, Sir David Campbell's regime will be associated with two things especially. The first is the difficult change, manifest in the Recommendations, by which the Council has restored a great measure of educational liberty to the medical schools, and has thus opened a new chapter in medical education in Britain. The second is the way in which the Council's disciplinary decisions, without losing any of their legal force, have been tempered always by professional understanding. In an appointment where it would be so easy to do no more than follow precedent, these are big things to have achieved.

In Lord Cohen of Birkenhead we welcome a successor who already has many achievements of his own.

Dr. G. F. ABERCROMBIE has been re-elected president of the College of General Practitioners. At the meeting last Saturday he was presented with his portrait, painted by Mr. Rodney Wilkinson.

From Words to Wards

6. REVOLUTIONARY POSSIBILITIES OF MODERN ARCHITECTURE

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ARCHITECTURE is altogether puzzling to many people. At one time their concern about it is emotional, and at others functional or technical or economic. This reflects the nature of architecture as an activity. Buildings must usually be constructed to a budget and to a time-table, be functionally efficient, and technically sound; and they end up as an environment which arouses various kinds of emotions and affective states. Modern architecture has revolutionised the possibilities for human environment, but it may be wondered what particular kind of change it represents that it could work a revolution, and what kind of revolution it has made possible.

The essential changes are perhaps most easily identified as a different attitude of mind and an increasing mastery of new technical developments. If a designer starts with a concept of what he wants a building to look like, he is likely to try to formulate his building to satisfy his objective, and the weight he gives then to requirements of function and design arising from the nature of his client's problems is likely to be diminished. This was a prevalent attitude well within living memory, and is still to be found. As often as not it was in the client's mind, if not in that of the designer. But the attitude which is at the heart of modern architecture is that the problem itself must be mastered first, with the aid of the technical potentialities of contemporary building; and the imagination is cultivated and disciplined as a process to operate within the framework thus created. The final outcome, then, imaginative as it may be, should not be a debased compromise between so-called " conflicting needs ", but an embodiment of specific requirements well satisfied in relation to one another, formed into an orderly, systematic design with character and other attributes of beauty. This is what is meant by a changed attitude of mind, though no doubt it often operates imperfectly among us. Medical people will themselves be familiar with parallel problems in coping with the impact of science upon their own sphere of activity.

All this perhaps needs some thinking about, and rather than embark on an elaboration of such quasi-philosophic matters at once, it will perhaps be better to enter this discussion through an example. I take one that results from newly emergent techniques and opens up new planning potentialities for hospitals, as well as for other building types—the technique of deep planning. It is perhaps the most significant recent development in building design, and has been made possible through improved illumination and ventilation techniques.

Deep Planning

If one depends upon natural light and ventilation only, the usable space in buildings is restricted to limited depths of the order of 25 or 30 feet from an outer wall. (I assume that we are considering multi-storey development: a single-storey building can be lit from the top). Consequently the large areas per storey which are often necessary in hospitals have tended to lead to long, thin buildings which have a relatively high ratio of external surface to contained space, with consequently relatively high sensitivity to losses and gains of heat, and relatively long communications, both for foot traffic and services. In principle a shorter and deeper building would be better in these respects, and if one such building were to contain what would otherwise be two or three long and thin buildings, there should be further gains along these lines. Quite possibly even the size of site required for a project might be reduced. Deep planning is therefore an important idea.

There is not yet wide experience of this technique in Britain, nor with hospitals anywhere. In America they have been exploiting its potentialities for offices and factories with success, and the results have given much food for thought. Fortunately research into some of the relevant technology is perhaps more advanced in this country, especially at the Building Research Station, than anywhere.

Illumination

The illumination problems are crucial, because the success of deep planning depends on producing conditions during daytime which do not cause people who have to work or stay some distance from the windows to feel at a disadvantage. A loss of contact with the outdoor world and complete dependence on artificial lighting are acceptable and often very welcome at night, but by day considerable psychological risks are often presented. In a department store, where the outer world is usually screened from view, probably to avoid confusion about colours and to make people satisfied to stay indoors for long periods, the large, lively, and changing indoor scenes seem to dissipate the risks.

A windowless factory is known to be still a somewhat problematical adventure, though a number appear to have been fairly successful. In a hospital a wholly artificial environment may be practicable, but it would seem to present considerable problems, and perhaps would only be considered in exceptional circumstances. On the other hand there seems reasonable confidence now that windows and artificial light can be used together to produce acceptable conditions for deep planning so far as many ordinary activities are concerned. The technique is to light artificially the region which daylight does not reach to a level which appears comparable with the brightness near the windows, with light of similar colour quality.

The phrase " appears comparable " is important. Here our concern is for the people who will be some distance from windows, who will look towards them and make involuntary comparisons, and these will not in fact so much concern levels of light as apparent brightness. In the interior of a building the brightness around a person will depend largely on the amount of artificial light and the lightness of the surrounding surfaces, but looking towards the windows they will see sky, bright outdoor views, and often shining reflections off the floors and furniture. In striking a balance between the peripheral and the interior conditions, then, the informed designer will probably do something to his window design to reduce brightnesses if for no other reason than to avoid having to use excessive levels of artificial light.

So far as character or quality of light is concerned, a very good mixture with daylight is of course obtainable from fluorescent sources, and if these are contrast-free in design, and light the ceiling so as to reduce contrasts

between source and the background against which they are seen, they will be relatively unobtrusive. By such means one can become surprisingly free of feelings of being dependent on artificial aids, provided that views through windows are preserved and the artificial lighting is sensitively done.

The windows are seemingly very important, for without them the feeling of enclosure can develop. Low sills and generous widths are desirable characteristics; but height is not. Slender window bars and frames, preferably white, reduce contrasts and give a good sense of contact with the outdoors—time-tested traditional techniques re-appreciated today. Coarse, dark, shadow-holding frames tend to inhibit the feeling of seeing easily through windows, and for reasons not yet clearly understood give rise to an impression of poor day-lighting. Patients may perhaps feel an uncomfortable sense of exposure if they are near large, low windows, and this presumably is a risk to be watched and offset; but with that proviso the generous view generally has the advantage that its value is felt farther within the interior of the building.

There will perhaps be some who still look askance at fluorescent lighting, recalling experiences of flicker and other discomforts. There need be no troubles of this kind, but there have been poorly designed fittings and installations in which they have occurred, and all that can be said is that it should not be so.

For some purposes tungsten lighting is very good, and occasionally a mixture of tungsten and fluorescent is worth using for really sensitive and flexible installations. There is nothing in this that is difficult for the good designer, and it should not detract from but rather underline my main argument, which is that the modern fluorescent source, used in association with well-designed windows, can apparently be used successfully to avoid feelings that only the areas near the windows can be really acceptable for living and working indoors.

Ventilation

This is not the whole of the technique upon which deep planning depends, for power-assisted ventilation is an equally necessary aid. This is not a euphemism for air-conditioning, although the latter involves powered movements of the air. It is a question of degree, for conditioning implies generally that it is processed: i.e., heated, cooled, washed, dried, sterilised—one or another or several such processes. Conditioned air is used in many parts of hospitals today, but the point that concerns the immediate question of deep planning is that it is impracticable to rely upon natural air movements for ventilation, while if power is applied, the ventilation problems can apparently be overcome satisfactorily.

Although not widely used here, air-conditioning has been well understood as a method of heating and ventilation by British engineers for a long time. The hospital problem is new to some extent in the complexity of situations where certain spaces must be exhausted direct to the open-air, where others must be pressurised, where yet others can have a normal flow through, or should simply have supplemented natural ventilation. To deal with such variety, while keeping the circuits systematic and sufficiently simple to control satisfactorily, requires a new measure of ingenuity in design and no doubt much remains to be learnt from experience and research; but the problems are being tackled, and if deep planning has in fact advantages for hospital design, then ventilation seemingly need be no bar to its use.

Potentialities

An obvious possibility for deep planning is in the type of ward-block where wards line the periphery of the building and enclose a core containing the ancillary services—the so-called race-track plan—which would depend for real success upon the use of this set of ideas. None of this type of ward has yet been built in Britain, but it is the subject of much discussion and some preliminary trials are planned. Caution is strongly evident in medical circles about any such innovation, not least because it is a revolutionary type of hospital mechanism. My intention here is, not to advocate it, but merely to illustrate the thesis that modern architecture has revolutionary possibilities.

Naturally some of the potential construction savings opened up by deep planning are absorbed by the engineering services necessary to make it work, and it is impossible to say yet where the balance of advantage and economy will be struck. However, with the gradual rise of technical standards, it seems likely that before long the costs of lighting and mechanical ventilation will lose weight as a factor in the larger assessment of whether or not the idea itself leads to a better or worse type of hospital. This is the important question.

Other Examples

If I were to venture on another example, I would look at the patient's environment—the problem of noise, of colour, and above all, of character, for there is no doubt that our grandfathers struck an institutional atmosphere with a skill that disconcerts and discourages us, while our fathers often achieved a feeling of asepsis that goes farther towards discomfort than we think wise today. Modern medical attitudes to quick recovery need a modern outlook upon building design for full success, and it is astonishing what can then be achieved, even in old buildings: wisely used colours, wallpapers, sound absorbents, and incidental planning improvements can almost work miracles that cost little beyond good judgment.

It would be foolish to suppose that every architectural innovation proves worth while, or that, because it is good in one type of situation, it will also be good in another. Curtain walls were introduced fifteen years ago partly because a thin metal-and-glass prefabricated skin seemed a way of cladding a building that had the character of modern industrial methods, and partly because they were light and quickly erected. The method was technically difficult, but it has been made to work, and it is liked. Yet there seems little doubt that it increases the sensitivity of buildings to external climatic influence and calls for more mechanical control of indoor climate than would otherwise often be thought necessary in our island climate. Its use for hospitals not otherwise likely to need air-conditioning ought perhaps to be looked at rather carefully.

The Future

The future is as difficult to foresee in architecture as in most fields involving science and technology, perhaps chiefly because we seem to be approaching a point where one might generally say that if a problem can be defined, and the solution is wanted badly enough, it can be solved. An architect has produced a scheme for an entirely glass-enclosed community north of the Arctic Circle in Scandinavia. It seems fanciful perhaps; but an air-conditioned street has already been built in Texas, and it is not so much farther to reach for a few streets, and

before long a town is within one's grasp. An air-conditioned town may be unlikely to appeal much to people in a temperate climate, but it does at least illustrate the forward architectural probes that the imagination is now able to envisage without losing hold of what is practicable.

Further revolutionary changes are likely to depend less on technical advances than on organisational advances. On the whole our technical resources are ahead of our use of them; for today it is more a question of what to do than of how to do it—of defining the problem, in fact.

A building is very much a joint product of the client and the designer. Not long ago a client, having selected an architect, would quite likely formulate instructions largely based on personal experience, and even quite a large building would not require a lengthy briefing period. Conventions would often pass unquestioned. But since the war the idea of research has so widely permeated our life and so sensitised us that it has become commonplace for both client and architect to do extensive studies of their problems beforehand. Scientists perpetually tour new laboratories to keep themselves abreast of fresh experience; medical people, industrialists, and others do the same. In some cases research and development programmes supplement or even lead this activity. We have, for example, the well-known work on laboratories by the Nuffield Foundation, and its even better known studies of hospital design problems. The development programmes in schools are famous, and much work on these and other building types has also been done at the Building Research Station.

All this work is informed by operational study. How is space used? Could some function be performed in a different and better way if a building were planned differently? What evidence can be obtained or deduced from experience? What trends can be identified which enable one to design for the future rather than the past? These questions represent the new approach by clients and architects to the problems of building and design.

We are nowhere near the climax of this new exploratory process, and indeed in some ways we are at a most uncomfortable stage of it. An immense amount of self-education is going on, but not a great deal of it has yet been systematised into ideas which enjoy a clear identity and general support, so that planning has little opportunity to settle down.

One consequence seems to be that, while there is much innovation on a small scale, the large, simple, deeply penetrating developments often escape us. This is least true of school design, where a close-knit group representing both client and designer has been able to lead the way into the best standards of schools in the world. It is substantially true of science laboratories and industrial buildings; and it is perhaps most true of all in the field of hospital design.

By general consent the major difficulty here is that too many people are participating in being the client. It is true that many have gone to some trouble to inform themselves, often meticulously; but collective decisions on major aspects are very difficult to establish, and moreover vary from one group to another, often radically, so that a hospital designed to the satisfaction of those who commissioned it in the first place seems a bad hospital to those who subsequently receive it for management and use, and who might have given a very different brief. This is sad, wasteful, and demoralising. The architectural possibilities become under these circumstances, almost entirely defined by the client, and revolutionary is not likely to be their outstanding attribute. Far greater resources than hitherto need to be devoted to the study of building requirements, notably through operational and sociological investigation.

Hospital design could particularly benefit from serious attention to this, for it is not the complexity of hospitals that presents the outstanding difficulties, but the divergent views which prevail among medical men about so many aspects of their design. For the benefit of the hospital building programme existing buildings might be examined more systematically for the experience they embody, and the multitude of new solutions now being formulated should be studied in order to diminish the uncertainties and differences of opinion that so often cause delay.

A few years ago the Nuffield hospital investigation gave us an excellent example of the kind of work that can usefully be done to develop planning ideas. Now we can hope that the development group of the Ministry of Health will be able to pick up the initiative; and no doubt the former leader of the Nuffield group, Prof. R. Llewelyn Davies, now at University College, will continue to contribute to this work. Even so the resources are far too limited; and if the revolutionary potentialities of modern architecture are to be realised in hospital design, it must largely be through close study of the requirements.

Conferences

MEASLES IMMUNISATION

FROM A CORRESPONDENT

IMMUNISATION against measles can be achieved by attenuated vaccine or by killed vaccine. Most work has been done with a living vaccine developed from the Edmonston strain of virus. At the International Conference on Measles Immunisation, held in Bethesda on Nov. 7–9, the experience with the chick-embryo strain, mainly Enders vaccine B, was described by S. L. KATZ Reactions were common and the main features were:

	Natural measles	*Vaccine*
Incubation	10–12 days	7 days
Catarrhal symptoms	Major	Minor
Communicability	Marked	Absent
Duration	7–11 days	5 days
Complications:		
Bacterial	5–15%	Absent
Central nervous system	0·1–0·25%	
Complement-fixing antibody response		97%

Rectal temperatures rose to 102°F or more in 80% and a rash developed in 45% of children. The vaccine disease was attenuated measles but too severe to warrant general use of Enders vaccine B. Modification of the disease with gamma-globulin had reduced reactions to negligible proportions. The gamma-globulin had to be given at a separate site and the dose adjusted so that it modified the measles but did not prevent infection. The antibody titres with combined active and passive immunity were slightly lower than with attenuated virus alone or after natural disease. The level of gamma-globulin required varied with the titre of measles antibodies. Commercial lots varied widely in titre, but approximately 0·01–0·02 ml. of gamma-globulin per lb. body-weight was the correct level if the titre was 1/4000 per ml. Katz found that titres of neutralising antibody after vaccination fell about fourfold in the first 6–12 months and then remained stable up to 3 years. M. HILLEMAN and J. STOKES found that maternal antibody inhibited the vaccine virus and they therefore recommended vaccination after 8 months of age. P. HALLONEN had used vaccine prepared by Lederle Laboratories from the

Enders Edmonston chick-embryo-adapted strain, with similar results.

F. R. McCRUMB reported the use of vaccine made by passaging Enders vaccine B in dog kidney. The results were very similar to those reported for Enders vaccine grown in chick-embryo cells both in severity of illness and consistency of antibody response. The human infectious dose was slightly less than 1 tissue-culture infectious dose by the subcutaneous or intramuscular routes. The vaccine was also effective when sprayed into the throat, provided about 1000 T.C.D.$_{50}$ were given. This vaccine was also used by intramuscular injection under the cover of gamma-globulin, and had been given in this way to about 4000 children. The vaccine virus was given in a dose of 100–3000 T.C.D.$_{50}$ with 12 measles neutralising units of gamma-globulin per lb. body-weight. On this schedule 10% of children had fever or rash.

Attempts to attenuate the virus were also described. A. P. GOFFE had grown Enders vaccine-B virus at 32°C in chick-embryo cells and used this in England. Reactions were considerably more severe than with Enders vaccine B. A. J. F. SCHWARZ had passed Enders vaccine B another 77 times in chick-embryo cells and in preliminary tests had produced a good serological response in 68 out of 70 children, but only 2 had a fever over 103°F (rectal).

Y. OKUNO described the use in Japan of a measles vaccine grown in FL strain of continuous human amnion cells and then passed 39 times in chick-embryo cells. After inhalation of 20 T.C.D.$_{50}$ 28 out of 31 subjects made a serological response. V. M. ZHADANOV reported results in Russia with a strain grown on monkey-kidney cells. This virus was much less virulent—indeed, probably too attenuated since 3 doses were required to give a 70% response. A. A. SMORODINSTEV's paper reported findings with the Leningrad IV strain grown on guineapig-kidney cells. The results were somewhat similar to those with Enders vaccine, and gamma-globulin was also used to modify the clinical responses.

I. ROSENTHAL found that approximately 50% of cases of normal measles show definite electroencephalographic abnormalities. The figure was up to 72% for 3-years-olds. About 3% of abnormal E.E.G. patterns persisted. In a small number of children examined, no changes were seen after Enders vaccine. C. P. HEGARTY found that no E.E.G. changes were observable in monkeys after administration of wild or attenuated strains; thus, the monkey is of little use for screening strains for capacity to produce encephalitis.

When the discussion turned to killed vaccine, J. WARREN described how virus was grown in monkey (cynomolgus)-kidney cultures and harvested when viral antigen was at a maximum. Virus titres of about $10^{4.5}$–$10^{5.5}$ T.C.D.$_{50}$ per ml. were obtained. Clarification of virus by filtration proved impossible so centrifugation was used. The virus was inactivated by 1/4000 formalin for 6 days at 37°C and at least 21 days at 4°C. Virus had to be concentrated about fivefold and incorporated with aluminium phosphate to give satisfactory antibody responses. With satisfactory vaccines geometric mean titres in guineapigs were about 1/100.

D. T. KARZON described a careful double-blind trial with this killed vaccine, started in March, 1961. 798 schoolchildren susceptible to measles were vaccinated with Warren's vaccine or placebo. There was a natural outbreak of measles almost simultaneously. After 3 0·5 ml. doses on days 0, 7, and 28, the geometric mean titre was only 1/19 but nearly all children had some antibodies. Despite this very low level of antibodies a substantial level of protein was noted. 2 weeks after the 3rd dose there was only 1 case of measles in a vaccinated child (at 72 days). The overall attack-rates were 19·2% for placebo and 6·1% for vaccinated. There was a 42% reduction in school absences among those vaccinated, compared with placebo children. The highest estimate of effectiveness was over 90% and the lowest 60%. Karzon pointed out that as the surveillance was limited to 2 months after vaccination it was impossible to say how long protection or antibodies would be maintained. H. A. FELDMAN reported results with an earlier vaccine also made by Warren. 72% responded to 3 doses but antibodies had largely disappeared in 5–6 months. Later he used a measles-poliomyelitis vaccine mixture incorporating a more virulent batch of measles vaccine. The antibody responses were: measles 100%, polio type 1 89%, type 2 100%, type 3 79%. Somewhat similar results had been obtained with a killed measles vaccine developed by Eli Lilly and reported by S. KARELITZ. This vaccine was also used with an adjuvant.

According to Feldman, reactions have been very mild with killed vaccine (after 1500 doses there had been febrile reaction in 4% and localised reactions in 2%), 3000 doses of Lilly vaccine produced reactions in only 1 child, who reacted after each dose. C. H. KEMPE reported a much higher reaction-rate.

DISEASES OF GENETIC ORIGIN

THE Postgraduate Medical Education Board of the University of Glasgow and of the Royal Faculty of Physicians and Surgeons of Glasgow held a conference on this subject on Nov. 15–17.

Prof. L. S. PENROSE briefly discussed the reasons for the growing importance of genetics—the disappearance of much infectious disease, the discovery of many genetically controlled biochemical lesions, the new chromosomal anomalies, and the improvement in methods of dealing with familial data. Clinicians needed the help of geneticists more and more, and it was important that they should speak the same language.

Neoplasia

Dr. W. M. COURT BROWN thought it important to distinguish carcinogens which acted chiefly as *promoting* agents (such as cigarette smoke) and those *inducing* agents which produced a primary genetical change. Of the latter the Philadelphia chromosome in chronic myeloid leukæmia was an example, though he thought this form of leukæmia might correspond to the precancerous phase of more conventional tumours. Cancer-susceptibility genes appeared to play a part in many tumours. He thought there might be relationships between the age distribution of cancer, the increase in chromosomal anomalies with age, the increased susceptibility to X-rays and perhaps other carcinogens with age, and the life-shortening effect of radiations.

Dr. C. A. CLARKE described an association, in two Liverpool families, between tylosis (palmar hyperkeratosis) and œsophageal carcinoma. Dr. A. M. VEALE reviewed the intestinal polyposes. There was some preliminary evidence for the existence of a " polyp " gene at the main locus which, when present together with the polyposis coli gene, caused early onset of cancer in that condition. Dr. J. A. MILNE described the familial benign self-healing squamous epithelioma of Ferguson-Smith; and the discussion was enlivened by the contributions of Dr. J. FERGUSON-SMITH himself.

Dr. J. A. BAIKIE showed that the familiar story of the Philadelphia chromosome and chronic myeloid leukæmia still held much of interest. He dealt especially with the terminal acute phase of this disease, when new races of cells arise: in one patient ten such races had been followed, each with its characteristic chromosome pattern and drug susceptibility. Prof. T. SYMINGTON discussed the varieties of the adrenogenital syndrome produced by three known enzyme defects, and the problems of diagnosis they raised. A group of male cases with these enzyme defects was probably being missed at present. He recommended the combination of Hall's ratio with the buccal smear as the most useful diagnostic routine in newborn children with doubtful genitalia.

Biochemical Lesions

Prof. G. PONTECORVO reviewed the parallel progress in several fields that has led to our present views of the nature of the genetical material. Genes as indivisible units strung together like beads were replaced by the linear array of morse-

code-like information units; vague nuclear proteins by the Watson-Crick halix; and "one gene, one lesion" by "one gene, one polypeptide chain". Now there was evidence, in some species, for genes that did not produce polypeptides, but regulated the rate of action of other genes. Dr. J. LEHMANN described the variations of hæmoglobin seen in the hæmoglobinopathies. The three normal hæmoglobins—A, A_2, and F—consisted of different combinations of four normal chains (α, β, γ, and δ). Since variations in the combination of chains occurred (and could be induced in vitro) a very few mutational variants in the chains could produce a great many different hæmoglobins. Dr. A. S. DOUGLAS reviewed the numerous known coagulation defects, and pointed out that most of the factors required in normal coagulation have been brought to light by their absence in the various genetically determined coagulation defects. In extensive surveys in the West of Scotland only three of these had so far been identified. Dr. A. GOLDBERG discussed the porphyrias; he found especially interesting the obscure relation between genetic and environmental causes in the cutaneous-hepatic form, and the diagnostic difficulties and variable inheritance of acute porphyria.

Aminoacid Metabolism

Dr. J. B. JEPSON reviewed the aminoacidurias. Our extensive knowledge was the result of Dent's choice of the aminoacids as the first compounds to investigate in urine by paper chromatography. Three very different biochemical lesions could give rise to aminoaciduria: accumulation due to metabolic block (as in phenylketonuria); failure of tubular reabsorption (either as part of a general defect of transport of the aminoacid, as in cystinuria, or as a specific defect of the renal tubule, as in Fanconi's syndrome); or indirect interference with tubular reabsorption by an unrelated metabolic defect (as in Wilson's disease and galactosæmia). In another paper, he described Hartnup disease, characterised by a pellagrous rash and excess of certain aminoacids in the urine, and showed how it had been proved that this, like cystinuria, involved defects of gut absorption as well as of renal reabsorption.

Dr. L. I. WOOLF described two very different leucine disorders. One was leucinosis ("maple-syrup-urine disease"), a classical metabolic block of the three branched-chain aliphatic aminoacids—leucine, *iso*-leucine, and valine—usually rapidly fatal and often missed. The other was leucine-sensitive hypoglycæmia, a treatable variety of "idiopathic" hypoglycæmia of infancy in which a protein meal of high leucine content stimulated insulin secretion.

Dr. J. D. ALLEN described arginino-succinic acidiuria, in which a block in the ornithine cycle produces mental defect and unusual hair growth. Prof. E. F. SCOWEN could not yet define the precise metabolic defect in oxalosis, though the excessive oxalic acid was probably derived from glycine via glyoxalic acid.

Prof. E. M. MCGIRR described the several distinct known forms of blockage or diversion in the pathway from circulating inorganic iodide to circulating thyroid hormone which could give rise to familial goitre or cretinism. A Scottish tinker group with much intermarriage had provided an interesting example of the dehalogenase defect. The nature of the associations with deafness and with ichthyosis was still uncertain.

Chromosomal Aberrations

Professor PENROSE reviewed the mechanisms by which congenital chromosomal anomalies could occur in man, and spoke in more detail of the role of maternal age in non-disjunction, of the existence of a familial tendency to non-disjunction, and of grandparental consanguinity in mongolism. Dr. M. A. FERGUSON-SMITH summarised the features of the principal syndromes arising from sex-chromosome anomalies in man, and discussed the active role of the Y chromosome in sex-determination. He supported the "single-X" hypothesis of the origin of both sex-chromatin and the polymorph "drumstick".

Mr. J. L. HAMERTON discussed mongolism and especially its inheritance. Even "regular" 21-trisomy cases had a small but significant familial distribution. Translocation mongols were proving to have a pattern of inheritance widely different from that originally predicted. With the commonest 13–15/21 type, female carriers had far too many affected and carrier offspring, and so far *all* the offspring of carrier males were carriers. Differential segregation in the ovum, and differential fertility of the spermatozoa, were among the possible explanations. Dr. J. H. EDWARDS reviewed other autosomal aberrations, especially the 17–18 trisomy. He stressed the caution needed when faced with a single case of congenital defect with a chromosomal anomaly: the chromosomal anomaly might be the cause of the defect, or it might be a non-significant variant. He gave as examples of such difficulties trisomy-22 and various partial trisomies. Dr. BERNARD LENNOX, required to review future possibilities in the chromosome field, hoped especially for technical advances (he thought pessimism over electron microscopy was premature), for the discovery of specific lesions like the Philadelphia chromosome in a few other tumours, and, ultimately, for the establishment of the gene content of each chromosome pair.

Single-gene Malformations

Dr. J. H. RENWICK explained that the reason for the geneticists' especial interest in such rare syndromes as were to be dealt with in this session was that the rarest syndromes were often inherited with the greatest regularity. He discussed the independence of variation in the different elements of many such syndromes, and questions of symmetry.

Dr. J. H. EDWARDS described several families with sex-linked hydrocephalus—probably the commonest single-gene form of hydrocephalus. A characteristic head shape and abnormally adducted thumbs were features. Mr. W. M. DENNISON demonstrated two familial syndromes seen in pædiatric surgical practice—short palate and atypical acrocephalo-syndactyly. He thought that surgical correction of severe childhood deformities might well lead to the recognition of more of them as familial. Mr. W. G. BROWNE described a large family with the "hereditary white mouth syndrome", with a conspicuous but asymptomatic epithelial thickening of the buccal mucosa inherited very precisely as an autosomal dominant. Finally, Dr. L. FISCH described the "white forelock syndrome" (or Klein-Waardenburg syndrome)—a triad of deafness, localised albinism (affecting especially the irises and the "forelock"), and inner canthus deformity, which is responsible for 2–3% of cases of congenital deafness. Prof. T. FERGUSON RODGER, chairman of the final session, echoing an earlier bon mot from Dr. Clarke, said that clinicians very commonly failed to recognise syndromes of genetic interest until they learned of their existence, and thought the conference would lead to increased recognition of many such conditions.

Medicine and the Law

Departure from Recognised Practice

IN March, 1949, a psychiatrist undertook the treatment of an intelligent single woman, then in her middle forties, with an anxiety neurosis.[1]

Between March and Aug. 6, 1949, twenty-four consultations took place in the doctor's consulting-rooms, analytical treatment being given about twice a week. By the end of July the patient, though much better, felt herself to be deeply in love with the doctor and told him that for that reason she could not continue with the treatment. The doctor thought that she was not yet well, and though the formal treatment ceased he continued to meet her between August, 1949, and March, 1950, taking her out to tea and dinner tête-à-tête in restaurants on a number of occasions, visiting her once at her home, a bed-sitting room, and also discussing a holiday together. By March, 1950, her condition had gravely deteriorated and the doctor

1. *See Lancet*, 1961, i, 610.

resumed psychotherapeutic treatment in his consulting-rooms in an attempt to dissolve the transference, but as it proved of no avail he brought it to an end. Her condition deteriorated further to such an extent that she became incapable of work, and she sued the doctor, alleging that her illness was caused by his wilful misconduct and professional negligence. Mr. Justice Barry absolved the doctor from all charges of professional misconduct but held that he had been negligent in entering into a social relationship with the patient between August, 1949, and March, 1950, and that that had resulted in the subsequent deterioration in her health. Mr. Justice Barry awarded the patient £6000 damages.

The doctor appealed, the issue in the appeal being limited to whether the doctor had been negligent between August, 1949, and March, 1950.

Lord Justice SELLERS said that it had not been suggested that the formal treatment given between March and August, 1949, was wrong, but there were dangers inherent in the deliberately invoked method of transference, and unfortunately the patient's attachment to the doctor in August, 1949, was complete and passionate.

The doctor had justified his continued association with her after that date on the ground that she was lonely and friendless and "not able to stand on her own feet". He had asked the court to treat the relationship of doctor and patient as still subsisting during the period August, 1949, to March, 1950, and to regard his meetings with the patient as a form of treatment directed to working out the transference. His Lordship found that a somewhat unreal position. In view of the judge's findings, those meetings had to be regarded as innocent social events and the real question was whether the social contacts were bad and negligent practice in the sphere of medicine in which the doctor worked. Whether that was so, and what effect it was likely to have on a woman in this condition, was a matter of expert evidence from those versed in this specialised branch of medicine.

It was the duty of a doctor to exercise ordinary skill and care according to the ordinary and reasonable standards of those who practised in the same field of medicine and surgery. It had been held that a doctor was not negligent if he had acted in accordance with a practice accepted as proper by a responsible body of medical men skilled in that particular art. His Lordship would add that a doctor might not be negligent if he tried a new technique, but the judge was right in saying that if the doctor did he must justify it before the court. If his novel or exceptional treatment had failed disastrously, he could not complain if it was held that he went beyond the bounds of due care and skill as recognised generally. Success was the best justification for unusual and unestablished treatment.

The medical evidence was all one way in condemning social contacts, and the doctor had failed to convince the judge that his departure from standard practice was justified and was a reasonable development in this young science. The judge was also justified in his view that the grave deterioration in the patient's health by March, 1950, was the consequence of that unwise treatment, which was negligent and in breach of the doctor's duty to his patient. £6000 damages was not excessive, and his Lordship would dismiss the appeal.

Lord Justice UPJOHN and Lord Justice DIPLOCK delivered concurring judgments.

Landau *v.* Werner—*Court of Appeal:* Sellers, Upjohn, and Diplock, *L.JJ.* Nov. 23, 1961. Counsel and solicitors: John Foster, Q.C., and John Spokes (Le Brasseur & Oakley); G. R. F. Morris, Q.C., and James Dunlop (David J. Griffiths, Bromley).

E. M. WELLWOOD
Barrister-at-Law.

Special Articles

CHILD PSYCHIATRY

THE Association of Undergraduate Teachers of Psychiatry, whose members include representatives of nearly all the undergraduate teaching schools in Great Britain and Northern Ireland, has sent us the following memorandum:

1. The responsibility for providing child psychiatric services is divided at present between the Ministry of Health on the one hand and the Ministry of Education acting through the local education authorities on the other. There are approximately 100 child psychiatric clinics which are solely the responsibility of the Ministry of Health. These are in general hospitals for the most part, and the majority of teaching hospitals provide such clinics. There are approximately 120 child psychiatric clinics which are the *joint* responsibility of the Ministries of Health and Education, and there are about 130 such clinics provided by the education authorities alone. There are thus more clinics for which the Ministry of Education takes responsibility (250), either jointly with the Ministry of Health or alone, than there are for which the Ministry of Health is responsible (100). The staffing structure and the orientation in these two groups of clinics is, in general, somewhat different. The "education" clinics are generally headed by educational psychologists who are full-time employees and may operate in a number of clinics in their areas. The psychiatrist in the team may be employed by the education department or may be seconded by the National Health Service for the work, usually on a sessional basis.

2. We consider that the term "guidance" is unfortunate in that, like marriage guidance and vocational guidance, it suggests an activity which can properly be carried out or supervised by those who are not medically qualified. We believe indeed that only a misunderstanding about the meaning of the word could explain the Ministry of Education's statement that "Child Guidance in the broadest sense is synonymous with education itself. . . ." [1] Most of us have been in charge of psychiatric clinics for children over a period of many years, and it has been our experience that most patients attending them have shown pathological anxiety with or without symptomatic behaviour disorder, physical symptoms, psychosomatic disorders, or psychoses; or have been below average intelligence. We have not seen many instances where "guidance" in any way covered the work that was done.

3. While it is generally true that drugs and physical treatments have a smaller place in the treatment of emotionally disturbed children than in adults, we believe that a knowledge of medical psychology, general psychiatry, and internal medicine is essential in those bearing the responsibility for diagnosis and the direction of treatment. For these reasons an educational psychologist and a pædiatrician without psychiatric training seem quite unsuitable as directors of psychiatric clinics. Yet both of these things occur whether or not the director is so described. At the same time we would not wish to seem to underestimate the vital roles played by psychologists and psychiatric social workers employed in a psychiatric framework.

4. We feel that a pædiatric hospital or the pædiatric department of a general or teaching hospital is always the ideal site for a psychiatric clinic, offering as they do the advice of colleagues and the usual hospital services.

5. We regret the dominant role of such bodies as the care committees of London which are under the control of the local education authority. This tends to exclude the general practitioner from the scene, to exclude doctors of the local health authority, and to destroy the confidence that parents should have that their affairs are secrets between them and the doctor.

1. Ministry of Education, circular 347, March 10, 1959.

Recommendations

1. The term "child guidance" should be abandoned and the alternative "child psychiatry" should be used in all cases.

2. The director of a child psychiatric clinic should in all cases be a consultant psychiatrist with experience of adult work.

3. A pædiatric hospital or department is the ideal site for a child psychiatric clinic, and the outpatient department should be supported by beds under the control of the psychiatrist.

4. We are firmly convinced that, at national level, child psychiatry should be the responsibility of the Ministry of Health.

5. We do not believe that child psychiatry is a legitimate preoccupation of the education authorities.

The memorandum is signed by Prof. Desmond Curran as chairman, and by Dr. Gerald Garmany (69, Harley Street, London, W.1) as hon. secretary.

GENERAL MEDICAL COUNCIL

THE Council met on Nov. 21. As has already been reported, Lord Cohen of Birkenhead was elected president from Nov. 28 in succession to Sir David Campbell, whose final presidential address was mentioned last week.

Lord Cohen presented the report of the Pharmacopœia Committee and the Pharmacopœia Commission. In order to secure that the metric system could take its place in the next *Pharmacopœia* it would be necessary to have statutory equivalents, so that if drugs were prescribed in the apothecaries system the pharmacist could dispense or supply preparations in metric units. The Weights and Measures Bill, in which an amendment to this effect was to have been introduced in the House of Commons, had lapsed. The leader of the House had suggested that the House might be too busy to deal with the Bill this session. Lord Cohen said that if the Pharmacopœia Commission and the Council could not be certain of an amendment by January it might be desirable to secure legislation on this one point.

The University of London has sought approval for the recognition by the Privy Council of the University College of the West Indies for admission of students for examinations for the degrees of M.B., B.S. of the university. Remarking that London University had allowed the Council very little time on this occasion, the President announced that the executive committee recommended that the Council should not offer any observations.

The President made a statement on reciprocity with South Africa. Under the Republic of South Africa (Temporary Provisions) Act, 1961, the arrangement for reciprocity between the United Kingdom and the Union which formerly existed under the Medical Act would continue in force until May 31, 1962. Under the Medical Act the Council could have reciprocity with either a Commonwealth or a foreign country, under conditions which were virtually identical. An order in council was needed for the purpose of applying to a country the relevant part of the Medical Act. These orders were made on the basis that the country offered just facilities for practice for doctors holding United Kingdom qualifications. Qualifications granted in the country had to be recognised on their merits by the Council. The executive committee looked forward to the continuance of reciprocity with South Africa. There was a little difficulty with regard to domicile: that had been adjusted by amendment to the Medical Act in South Africa. Possibly the Privy Council would deem it necessary to make a new order applying the Medical Act to South Africa as a foreign country. The only difference would be that after next May those who applied would be registered in the foreign list instead of the Commonwealth list. "I should add that the privileges conferred are the same whether the name is on the Commonwealth list or the foreign list."

Finally, Lord Cohen moved a resolution to record the feelings of deprivation which members felt at the retirement of Sir David Campbell—member since 1946, president since 1949, and chairman of the Medical Disciplinary Committee since its inception. Sir David was the first president to have visited medical schools in all parts of the Commonwealth on behalf of the Council. Sir David replied that the presidency of the General Medical Council was the highest honour a doctor could come to, but it was also a great responsibility. The happiest side of his presidency had been the educational work: the least pleasant side was the disciplinary one, because in the interval between sessions the president often had to take grave decisions, and, in making those decisions, the president was sometimes a very lonely man.

Medical Disciplinary Committee

THE Medical Disciplinary Committee met on Nov. 22-25, under the chairmanship of the president, Sir David Campbell.

APPLICATIONS FOR RESTORATION

The committee directed the registrar to restore the name of *John Bodkin Adams* but did not direct him to restore that of *Edward John McCann*.

CASE CLOSED

The registrar was not directed to erase the name of *John Anthony Perpoli*, M.C., registered as of 11, Bank Street, Hillhead, Glasgow, W.2, L.R.C.P.E. 1939, against whom judgment had been postponed following convictions for driving a motor-car when under the influence of drink.

JUDGMENT POSTPONED

Henry Joseph Caron, registered as of The Surgery, Tyntyla Road, Llwynypia, Rhondda, Glam., L.A.H. Dubl. (1949), appeared for judgment, which had been postponed for one year following a conviction in 1960 at Ystrad magistrates' court of eight charges of unlawfully procuring dangerous drugs. He now admitted a further conviction on July 17 at Liverpool magistrates' court of being drunk and disorderly in a public place, for which he had been fined £1. Mr. G. J. K. Widgery, solicitor to the Council, said that on Sept. 7 last at Windsor magistrates' court Dr. Caron pleaded guilty to two charges relating to obtaining 'Drinamyl' and 'Sodium Amytal' tablets and was granted a conditional discharge. Judgment was postponed for a year.

The committee decided to postpone consideration of the case of *William Quirke*, registered as of Mountjoy Lodge, Kildare, L.M.R.C.P.I. (1949), who was summoned to appear for judgment postponed from November, 1960, when he had been found to have been convicted on two charges of obtaining dangerous drugs by false pretences. Mr. Widgery said that there had been a further conviction and Dr. Quirke had been placed on probation for three years.

Roy Wilfrid Downie, registered as of 88, Comely Bank Avenue, Edinburgh 4, M.B. Edin. (1944), had two convictions relating to drugs. On June 30, 1960, at Wolverhampton magistrates' court, he had been convicted on six charges of

unlawfully procuring dangerous drugs and fined £150 and ordered to pay £1 for costs. On Dec. 20, 1960, at Rochdale magistrates' court he was convicted on nine charges of unlawfully procuring dangerous drugs and two of failing to make entries in his dangerous drugs register and sentenced to eight months' imprisonment, which was reduced on appeal to a fine of £330. Judgment was postponed until November, 1962.

ALLEGED ADVERTISING BY PLASTIC SURGEONS

The committee spent three days considering a case in which seven leading plastic surgeons were accused of advertising.

Richard John Vulliamy Battle, registered as of 7, Fife Road, London, S.W.14, M.R.C.S. (1931), F.R.C.S. (1933), B.CHIR. Camb. (1933), *Patrick Wensley Clarkson*, M.B.E., registered as of 107, Harley Street, London, W.1, M.R.C.S. (1935), F.R.C.S. (1936), M.B. Lond. (1940), *William Goldthorpe Holdsworth*, registered as of 138, Harley Street, London, W.1, M.B. Melb. (1933), F.R.C.S. (1943), *David Napier Matthews*, O.B.E., registered as of Foley House, East Heath Road, Hampstead, N.W.3, M.R.C.S. (1935), F.R.C.S. (1936), M.B. Camb. (1936), *Arthur Rainsford Mowlem*, registered as of 149, Harley Street, London, W.1, M.B. N.Z. (1924), F.R.C.S. (1929), *Joseph Patrick Reidy*, registered as of 144, Harley Street, London, W.1, M.R.C.S. (1932), F.R.C.S. (1941), M.B. (1937), M.D. Camb. (1959), and *Raoul Peter Gauvain Sandon*, registered as of 17, Langley Avenue, Surbiton, Surrey, M.R.C.S. (1941), F.R.C.S. (1951), M.B. Lond. (1949) were charged (1) that they combined together and with other persons unknown (being members of the British Association of Plastic Surgeons) to advertise for patients in the manner set out in the particulars; and (2) that each severally (*a*) had advertised for patients in the manner set out and (*b*) had sought to profit by the publication of the matter referred to and had shown himself prepared to accept patients notwithstanding that he knew that such patients had been induced to seek his services in the circumstances set out: and that in relation to the facts so alleged each one had been guilty of infamous conduct in a professional respect.

Mr. Peter Boydell, instructed by Waterhouse and Co., solicitors to the Council, said the committee would hear from the evidence that at many points the facts of this case would echo the case of Dr. Gardiner.

In the issue of *Woman and Beauty* dated October, 1954, there appeared an article, entitled "Women and Plastic Surgery", which stated:

"In an age of many wonders, perhaps one of the greatest of them is plastic surgery. With the experience gained from the miracles of skin grafting and surgery done during the war, plastic surgery is now very far advanced. It is a branch of medicine about which everyone should know some of the details, so that they can appreciate its possibilities. It is not only surgery, it is an art which, when practised by skilled hands, performs marvels of transformation.

"Being out of the ordinary run of surgery, it is a profession which inevitably attracts charlatans. There is no law to prevent any man setting up as a plastic surgeon, but if anything untoward happens, the patient has no redress. In any case, it is very necessary to be sure you have the services of a qualified man. Anyone can find out the qualifications of a surgeon by applying to the British Association of Plastic Surgeons, c o Royal College of Surgeons, London W.C.2. Your own doctor should also be able to recommend a good plastic man or you can find one at most of the big hospitals.

"FRCS are the letters which proclaim a surgeon, but all surgeons specialising in plastic operations have had to do three or four years extra training after their general surgical training in order to learn the technique of this particular branch of surgery."

Mr. Boydell said the article was published with the agreement of the British Association of Plastic Surgery. The "torrent" of letters which resulted from the article were sent to the Association. Mrs. Gardiner, wife of Dr. Gardiner, wrote to the Association in the name of her sister, Mrs. Ewing Evans, and received a reply listing nine London teaching hospitals.

In 1959 a further article, "Operation Beautiful", appeared in *Woman's Own*, which stated:

"... She saw her own panel doctor, who confirmed that though 'cosmetic' operations *are* sometimes done through the National Health Service, this is rare. Her own nose, much as she hated it, would not be likely to qualify for such free treatment on 'psychological' grounds. It was a clear case of save up—or do without.

"Then and there, Barbara began to save towards her target—at least £150 to cover the fees for the operation and anæsthetic, plus a week's nursing care."

The article invited readers to write for a pamphlet, also entitled "Operation Beauty". This stated:

"But let us speak plainly. Plastic surgery is an operation. No operation is pleasant, however minor. Plastic surgery is expensive in terms of money, although it is cheap in terms of the happiness it can bring ...

"Very few cosmetic operations can be done on the National Health Service; and only your doctor can advise you. In the same way, your own doctor is the one to put you in touch with the most competent plastic surgeon for your case—it is, of course, vitally important to approach one who is fully accredited.

"There are, however, some more conservative doctors who are not sympathetic to cosmetic surgery and yours may be one. If this is the case, and you still feel you would like to consult a plastic surgeon, you can write, enclosing a stamped addressed envelope, for a list of accredited specialists in your area to:

The British Association of Plastic Surgeons,
47, Lincoln's Inn Fields, London W.C.2."

As a result of this pamphlet, Mrs. Gardiner wrote to the Association and received a list containing the names of Sir Archibald McIndoe and the seven practitioners. In one section of the list of members there were set out the names of those practising in London: at that time there were 22 full members and 36 associate members.

Mr. Boydell then read a letter from Paris sent to the practitioners by Mrs. Gardiner's niece, Miss Mary E. J. Evans:

"Dear Sir, I have been given your name by the British Association of Plastic Surgeons, whom I wrote to on the advice contained in the pamphlet 'Operation Beauty' circulated on request by the magazine *Woman's Own* to their readers.

"I am an English girl studying in Paris and I would like to have the shape of my nose improved by cosmetic plastic surgery.

"I shall be returning to London for two weeks on November 14th.

"I should like to know your fees for this operation and whether you would be able to operate on me at this time.

"P.S. I greatly admired the nose illustrated in this article on cosmetic plastic surgery in *Woman's Own*, and I would like to know whether you are the surgeon who performed this operation?"

"The replies came with commendable speed from all seven practitioners," continued Mr. Boydell. He read the replies, signed by the surgeons or their secretaries. He said Mr. Mowlem said he was the only one who said he did not see Miss Evans' letter.

The first witness for the Council was Miss Ruth Jordan, editor of *Woman and Beauty* when the article appeared. She saw Sir Archibald McIndoe at the London Clinic. At his suggestion she afterwards saw Mr. Reidy. Asked who suggested the sentence: "Being out of the ordinary run of surgery, it is a profession which inevitably attracts charlatans", Miss Jordan replied: "I think Sir Archibald checked the article."

Mrs. Anne Doreen Gardiner, wife of Leslie Elgar Gardiner, said in evidence that Mrs. Ewing Evans was her sister. She could not remember whether she or her sister wrote the letter: if she did it was with her sister's permission. She was asked by the General Medical Council to produce evidence on oath. She agreed that at that time her husband's name had been erased from the Register for advertising.

Leslie Elgar Gardiner gave evidence of correspondence which he had had with Mr. Mowlem in 1959 about publicity.

"The publicity I am concerned with is not, as you state, unwanted," Mr. Gardiner wrote to Mr. Mowlem, "but instigated and fostered by certain members of the BAPS, using the association as a cover for their activities. It is further complicated in that they are not, as one might imagine, insignificant names.

"You say that you too deprecate this publicity and think that good surgery needs none. Here I must make it clear that it is not the

publicity that I deprecate but the restrictive trades union method employed and in particular its effect upon my practice now and in the future."

Mr. Mowlem replied:

". . . . I am at something of a loss to understand how I can assist, since I have no knowledge of the 'facts' which you tell me exist.

" In any case you will appreciate that the British Association of Plastic Surgeons is not a disciplinary body and that it can exercise no control over its individual members unless they have been proved guilty of some misdemeanour."

Mrs. Phyllis Digby Morton, consultant beauty editor of *Woman's Own*, said that she wrote the article and the leaflet "Operation Beauty". About a week after the pamphlet appeared she received a telephone call asking for the name and address of the British Association of Plastic Surgeons to be removed, and she did so. She had sent the leaflet but not the article to the Association for checking. She agreed that in writing the leaflet she had considerable cooperation with Sir Archibald McIndoe, who was a friend of some years' standing. He suggested sending the leaflet to the Association.

After the committee had heard submissions by lawyers for the defence and Mr. Boydell in reply, the Legal Assessor, Mr. C. P. Harvey, Q.C., advised the committee that count one was an allegation which, in the criminal courts, could be regarded as something like conspiracy, and there was no evidence proper to their consideration on this charge in respect of Mr. Clarkson, Mr. Holdsworth, and Mr. Matthews. After consideration in camera, the Chairman announced the committee's finding that these three practitioners were not guilty on this count. The committee did not uphold the other submissions that there was no case to answer.

Mr. Charles McLaughlin said that he was honorary secretary of the Association from 1957 to 1959. He devised a standard letter to be sent to members of the public who wrote asking for details of plastic surgeons. Where possible always more than one name was included: that might occasionally not be possible in some remoter parts. The names were those of full members who were consultant surgeons and who would be, if necessary, available for private consultation. There were about 22 full members in London, and they were split quite arbitrarily into two lists to be sent out at random by the secretariat. Qualifications for full membership were that a surgeon should hold the fellowship, have had four years' training in general surgery, and subsequently further training as registrar or senior registrar in plastic surgery. These requirements had been recognised by the Ministry for consultant appointments under the National Health Service. He had only checked the *Woman's Own* pamphlet for clinical details.

Prof. T. Pomfret Kilner said he had been president of the British Association of Plastic Surgery, and was a member of the General Medical Council. When he was president of the Association in 1955 he was aware of the practice of giving the names of plastic surgeons to inquirers. He did not see anything unethical about it. " I am still of that opinion," added Professor Kilner. The ideal was that the approach should be through the general practitioner, but he did not think that would be sufficient for every patient in every kind of circumstance.

Mr. Battle said that he discovered in 1954 that the Association gave inquiring patients lists of surgeons or hospitals. He did not regard the practice as unethical. He only saw the pamphlet " Operation Beauty " after he had received the " provocative letter " from Miss Evans. This letter he had regarded as a routine inquiry. He sent her a factual reply. His letter was not an invitation to Miss Evans to become a patient.

Mr. Clarkson said that he had known for some years that it was the custom to supply names to the public. He knew it was a matter of issuing, not individual names, but some impersonal alphabetical list including all the names.

Mr. Holdsworth said he was not aware that the Association was accustomed to send out lists of surgeons in response to requests from the public. He did not think it wrong to answer Miss Evans's letter, because he regarded his Association as a highly respectable body.

Mr. Matthews said that the first he knew of the practice of the Association of sending out his name on a list was when he received a copy of the list from solicitors. He at once wrote to the Association stating that in no circumstances must his name be given to lay inquirers. It was his practice to ask patients to bring a letter from their doctor when they came. If they did not he asked them the name of their doctor. A small proportion would not give it. The proportion of those coming for cosmetic surgery who did not want to give their doctor's name was larger than for other surgery. He now no longer saw such patients, but some were in very genuine distress and it seemed wrong that he should not be able to help them.

Mr. Mowlem said that he had gone to very considerable lengths to avoid publicity. He had no knowledge of the *Woman and Beauty* article. When he learned that lists were being sent out he drafted a letter immediately to the secretariat that the practice should stop until it had been considered by the council.

Mr. Reidy said he had not inspired press articles and had nothing to do with the preparation of the *Woman and Beauty* article. The practice of answering letters from the public existed when he took office as honorary secretary.

Mr. Sandon in his evidence said that advertising had never been discussed at any meeting of the Association. Asked why he sent a telegram in French to Miss Evans, he said he merely sent it to ask whether she proposed to come.

After the committee had deliberated in camera the chairman told the practitioners;

" The committee have found that none of you has advertised for the purpose of obtaining patients as alleged in the charge, and accordingly that none of you has combined to advertise. The committee have, however, found it proved that you have shown yourselves prepared to accept a patient notwithstanding that you knew that the patient had been induced to seek your services in the circumstances alleged in paragraph four of the particulars; but this finding of fact is, in the opinion of the committee, insufficient to support a finding of infamous conduct in a professional respect. The committee have accordingly recorded their finding that you and each of you is not guilty of infamous conduct in a professional respect in relation to any of the matters against any of you in the charge.

" The inquiry, however, has disclosed a state of affairs which the committee could not view without serious misgiving. In particular the committee have noted with much concern the following circumstances:

" (1) Officers or members of the British Association of Plastic Surgeons have, wittingly or unwittingly, cooperated in the publication in the lay press of articles calculated to stimulate members of the public to apply to the Association for information about the services of plastic surgeons.

" (2) the Association have subsequently made available to persons who applied to them as a result of such articles the names of a limited number of plastic surgeons, all members of your Association.

" (3) Members of the Association have been prepared to accept patients who had been led to seek their services in this way.

" The committee are concerned that members and officers of an Association of specialists should at any time have lent themselves to such practices. The committee trust that note will be taken of these proceedings, and that there will be no recurrence of the events."

After judgment had been given, Mr. Boydell made a statement correcting what he had said, in opening the case, about who was the complainant. The first approach was made by Mr. Ludivicki, who said he was a friend of Mr. Gardiner. As a result of what he said, Mrs. Gardiner made a statutory declaration; " and so far as I know she and she alone made it," said Mr. Boydell.

In England Now

A Running Commentary by Peripatetic Correspondents

Now that we have done a survey of our own we shall never again be able to glance casually at the results of a follow-up. Instead we shall remember the mounting excitement when all but 2 of 164 British children in a long-term follow-up had been traced and how each new "recovery" was a cause for celebration. The penultimate, who lived in New York, would reply to no correspondence. His surprise when I dropped in on him in Brooklyn to pay a personal visit was understandably great. He had the impression that the follow-up service of our hospital was unique, and it did not seem necessary to point out that a meeting of the National Nephrosis Foundation was taking place a few hundred yards away from his home on the same day. He had not replied to letters lest the U.S. immigration authorities found out about his previous ill health. The last case of all we had given up; but, thanks to her unusual name, a photograph of her wedding was recognised by a socially minded almoner on the very day that her name was changed. We could hardly wait for her to return from her honeymoon to add her to the collection and celebrate the 100% follow-up in the appropriate fashion.

* * *

The other day it took two adults and one girl three-quarters of an hour to catch one mouse. At the end, all the study furniture had been moved, and the hall was in confusion. The next mouse was found by the cat, who dislodged it from the curtain with one pounce and caught it with the second, the whole process taking under five seconds and causing no disturbance.

Moral—Don't do it yourself: always call in a specialist.

* * *

As psychiatrists we still complain about the public attitude towards mental illness and the stigma that attaches to the psychiatric patient. Today one of my patients told me I had insulted her by calling her a neurotic when, "as everybody knows, a neurotic is someone who should pull herself together and whose symptoms are her own blame and nothing but imagination." Maybe we should start our propaganda nearer home.

* * *

The recent grant of arms to the College of General Practitioners must have pleased many people. But how many readers noticed the differences between the descriptions in two weekly medical journals? What can we learn of the two editors from the ways in which they treated the story?

Editor A, for example, is clearly not a Bart's man: he refers to St. Bartholomew's Hospital, London, whilst B has omitted the name of the capital, assuming that all the world knows where Bart's is. The two editors react differently to the Apothecaries, A alone informing his readers that it is the London society being referred to, but, unlike B, omitting their proper epithet "Worshipful". Neither editor tells us where the Royal College of Nursing is to be found, but both refer to the Barber Surgeons of London.

The two editors differ in their attitude towards medicine: B does not share A's view that the G.P. of today uses "an opium poppy and a gentian" in his daily practice (or does he think it too obvious to need mentioning?); on the other hand he alone refers to the miraculous and protective powers of the unicorn's horn. But A likes animals: to him the lynx is "he", though merely "it" to B. But if we want real insight into the characters of the two editors we must study their attitude towards punctuation. A likes quotation marks and commas: B likes hyphens and capitals.

* * *

Our family tour through Italy was delightful but I did just wonder about the impact of all those Florentine statues on the minds of our overdressed children. Our daughter, aged 10, contemplated Michaelangelo's David from all sides and then came up with the breathless announcement, "What fingernails! What fingernails!" I checked. She was right, there were fingernails. That there was more than fingernails, however, emerged when we came home and had all our photographs developed. From her camera came a picture of Fenton (age 6) posing as David on a Florentine veranda.

* * *

I picked him up, complete with trade plates, on the North Circular a couple of miles out from Kew Bridge, and took him up to Doncaster, where he was to collect a new car and ferry it back to Guildford. A large, cheery, red-faced man, no sooner had he settled himself than he dug a hand into the pocket of his weathered overcoat, produced two aspirin tablets, and ate them dry. "Some people," he said, "don't like the taste of them, but I don't mind them at all. Been taking them a few days now. Had awful toothache. I think they're doing a bit of good though." Clear of Mill Hill, we fastened our safety belts, and he soon slept; and so we hurtled northwards on the new double track of A.1. High winds pushed at the car, bright sunlight flooded in, and sudden rain squalls ridged the windscreen. Rainbows arched in the sky, and the ferryman slept, and woke, and slept again. We stopped briefly for a meat-pie and a cup of tea, the café a mere hutment surrounded by heavy wagons parked upon the gravel around. Here in the "caf", haven of the long-haul men, the room rocking with a beat-tune from the juke-box, a latter-day Cleopatra, between tea-urn and sausage and chips twice, held her court. My passenger had more aspirin with his tea, and also tonic tablets which, he said, he and his wife found very steadying for their nerves. He accepted a cigarette. "Yes," he said, "I smoke these now myself. Remember that smog a bit back that killed thousands? Well, I was nearly one of *them*. Had pneumonia, you know, and oxygen and all that. So after that I thought 'this is where I'll have to make a change', and I've smoked these little 'uns ever since." In Doncaster it was the children's coming-out time, mums waiting with prams and white-coated traffic wardens hovering. I left him at the factory gates, his face beaming, delighted at having time unexpectedly on his hands, pleased at the thought of getting home to bed before morning.

* * *

The matriarchy of the hospital has nothing on the matriarchy of the modern air-line. We are collected, ever so politely of course, into the nursery by nanny's insistent tones over the intercom. We wait for nanny to arrive. Usually she is quite pleasant to look at, so we forget to throw a temper tantrum and follow her obediently into the bus. It is too far for the toddlers to manage on foot, but we are only going across to the plane—that is, of course, when nanny is happy that we are all here. Then we are all out again, watched now by an assistant nanny, and take our seats. We sink into our womb-like enveloping chairs, supporting limbs and trunk in any position we like—amnion by courtesy of 'Dunlopillo'. Nanny prepares her tray of sweets—one for each of us—no favouritism. Relax children, you are being taken care of.

I forget the name of the air-line I flew with last, but they at least were enlightened enough to know what they were doing. As I sat in my chair, with nanny coming towards me, I looked up to the illuminated sign over the door. I don't think anyone had been playing with it, but I am sure it said PLEASE FASTEN YOUR UMBILICAL CORD.

* * *

From a collection of Psacred Psalms For Psychiatrists without many apologies to the Rev. Isaac Watts.

When Michael Ashby did aver
That birching, blood, and canes
From crimes of violence would deter
The criminals with pains,

Then Stafford-Clark, irate and strong
With facts and sense and power
Exposed him futile, proved him wrong.
This was Clark's finest hour.

The good he did, not long will live,
As he himself does know,
Yet praise and thanks to him I give
Which in this psalm I show.

Letters to the Editor

RECONSTRUCTING THE N.H.S.?

SIR,—It is particularly unfortunate that non-medical critics of national health services, both in Britain and elsewhere, ignore the basic fact that, in medical care, we are selling goods to blind customers. Dr. Lees' statement quoted by Dr. Searle (Oct. 28) (" Medical Care is a personal consumption good, not markedly different from the generality of goods bought by customers ") is completely wrong and accounts for the basic mistakes of so many laymen who try to evaluate medical services. As any practising doctor knows, the patient judges the service very superficially. The dissatisfied patient may have been served extremely well and the satisfied and often effusively grateful patient may have suffered many errors in diagnosis and treatment. The patient just has not the knowledge to evaluate the service.

The emotional and intensely personal factor in disease makes the supply of medical services totally different from that of any other commodity. The increasing faith in the successful treatment of everything, and the materialistic outlook of modern society, gives steadily increasing pressure for the provision of more expensive services. No-one with any knowledge of social medicine will doubt that the cost of these services will rise, if money is made available, since the saturation level has not been reached—if it ever can be. Whether the money is being spent wisely is another matter, but the economist must, I am afraid, accept that at the moment we cannot directly measure the total value to the community of increasing the medical services. Much of the return from the British National Health Service has been in reducing the amount of unhappiness that previously surrounded those who were unable to obtain the best available treatment for either themselves or their dependents. The vast amount of minor, but partly incapacitating, ill health is borne with fortitude by a community with insufficient service, and they are relieved to some extent by improving the availability of medical care. This gives rise to the paradox that more sickness can be measured as one improves the level of medical care.

Too many critics are fit people who have little need at the moment for medical care and begrudge paying taxes for those who do. I am sure the aged and infirm would vote wholeheartedly for comprehensive " free " medical care provided from taxation, even in its present imperfect form, rather than return to the state of fear of having inadequate insurance cover for all eventualities. It seems difficult to believe that really comprehensive cover for those who want to pay by personal insurance, plus State cover for those who have not bothered to pay, can in the long run be any less expensive unless one is determined to deprive the thoughtless, the feckless, and their dependents of anything more than a primitive life-saving-only type of medical care. Will mammoth insurance companies be any more free of economic pressure than State departments? A tie-up between insurance companies and large pharmaceutical combines could really put medicine into slavery.

University of Otago Medical School, Dunedin. C. W. DIXON.

FROM WORDS TO WARDS

SIR,—In thanking Mr. Brand (Nov. 25) for his generous estimation of my article, The Planning Process (Nov. 11), I of course agree with him that the treatment of patients is the primary aim of every hospital, whether teaching or non-teaching; in fact, I had hoped I had made this very point in describing the set-up of the building committee responsible for the new St. Thomas's. But if I failed, may I now amplify what I then wrote by saying that the first consideration that should be in the mind of the successful hospital designer is that he is building for people—not sick people only but those who treat them—and that the human scale must be preserved throughout.

London, W.C.2. IAN M. LESLIE.

URETHRAL CATHETER AND URINARY-TRACT INFECTION IN PREGNANCY AND PUERPERIUM

SIR,—The paper by Dr. Brumfitt and others (Nov. 11) is of much practical interest and we have recently concluded a similar study.[1] We would like to comment on two facets:

(1) The authors state that a good response to chemotherapy was obtained in their patients who developed bacteriuria. As all their infected patients apparently were treated there is no telling what would have happened without treatment—particularly in the asymptomatic group. In our bacteriuric women (> 100,000 organisms per ml.) who developed infection in hospital, only 22% still had infection six weeks later without any treatment at all. It is believed that at the present time asymptomatic bacteriuria *alone* should be watched rather than treated, until evidence is available that the bacteria are really harmful to the patient.

(2) The high incidence of infection (22·8%) in the group-III cases (those in whom catheterisation was required on clinical grounds) was assumed to be due to the catheterisation. As there are no controls for this group—i.e., patients with the same complications but who were not catheterised—it seems inadvisable to conclude that the high incidence of infection was solely due to the catheter.

We agree that unnecessary catheterisation should be avoided; but a single catheterisation in healthy pregnant women at term usually produces only a trivial short-lived bacteriuria. This happy outcome does not of course necessarily apply to other population groups or to other stages of pregnancy.

Departments of Medicine and Obstetrics, Montreal General Hospital, Montreal, Canada. MICHAEL KAYE
J. DE VRIES
K. T. MACFARLANE.

LATE APPEARANCE OF LEG SYMPTOMS IN PULMONARY EMBOLUS

SIR,—The article by Dr. Stevens (Nov. 4) is of great practical interest. For us, the article was very timely, because we saw a similar case in the chest unit of this hospital.

A 46-year-old housewife was admitted with 2 days' history of right-sided chest pain and pyrexia. She had had a hysterectomy for uterine fibroid six weeks before admission. Three weeks later she had sharp pain in the right chest for a few hours. On admission she looked ill, and her temperature was 101°F and respiratory rate 24. Resonance was impaired in the right lower chest, and a friction rub was audible in the same area. Chest X-ray showed some haziness in the right lower lobe and a small pleural effusion. Her leg appeared normal, and Homans' sign was negative. We treated her with bed rest, analgesics, and a five-day course of tetracycline (1 g. daily). Her chest symptoms had then completely disappeared.

On the seventh day in hospital she had pain and swelling of her left thigh, and a typical picture of thrombophlebitis was noted. She was treated with anticoagulants, and her leg improved.

We report this case as another example of late appearance of leg symptoms about four weeks from the initial pulmonary

1. *Canad med. Ass. J.* (in the press).

embolism. We want to emphasise Dr. Stevens' view that even in the absence of leg symptoms all cases of clinically suspected pulmonary embolism should be treated by anticoagulants, which will protect the patient from further embolism from a silent focus.

Springfield Hospital, Grimsby, Lincs. JOHN GLEN
NIRMAL K. MAJUMDAR.

ABSENCE OF ESSENTIAL HYPERTENSION

SIR,—The interesting work of Dr. Maddocks (Aug. 19), about the possible absence of essential hypertension in the population of the Gilbert Islands, is consistent with our hypothesis [1] that the variation of the frequency distribution curves of arterial pressure in a population sample is directly influenced by the intensity and duration of environmental factors and is irrespective of age.

In his fig. 3, Dr. Maddocks compares a tension curve of a female population aged 50–59 in the Gilbert Islands and a curve for London females of the same age and sex. The Gilbertese curve has a positive kurtosis (degree of "peakedness") and the London curve is flatter and shifted to the right with a negative kurtosis. Fig. 4 of our work [1] showed the same results when we compared a sample of an aged Indian Andean population of Macusani, Peru, with a similar English male population. Our Macusani tension curve is similar to the Gilbertese one of Dr. Maddocks; despite the age of Gilbertese the curve has a young shape with positive kurtosis, because the islanders have not yet been exposed to the strong environmental influences of western civilisation. The Gilbertese curve has a mean systolic pressure of 125, against only 115 of our Macusani curve. This difference may be due to the influence of "Western" culture. The population of Macusani in the eastern Andes is completely isolated from the modern world and has never known war. The Pacific islanders have been less fortunate: for example, the island of Abaiang, whose total population was measured by Dr. Maddocks, is very near the atoll of Tarawa, where one of the bloodiest battles of the Pacific war was fought in November, 1943.

Hospital J. J. Aguirre, University of Chile School of Medicine, Santiago. RICARDO CRUZ-COKE.

POLYMYALGIA RHEUMATICA

SIR,—I was interested to read Dr. Todd's article (Nov. 18) and I agree with him that this common, benign condition is probably a variant of rheumatoid disease. My own view has always been that this syndrome is a *forme fruste* of rheumatoid arthritis, since the symptoms and signs are virtually identical with the prodromal symptoms of rheumatoid arthritis before joint involvement.

Like Dr. Todd, I disagree with the view of Paulley and Hughes [2] that "polymyalgia rheumatica" or, as I have termed it "anarthritic rheumatoid disease" is giant-cell arteritis in disguise.[3] I have now followed up my original 50 patients [4] for an average period of over eight years and none have developed eye symptoms, whereas 39% of Paulley and Hughes, patients and 62% of Ross Russell's series [5] developed ocular manifestations. The mean age at time of onset for my series was 60·8 years, whereas the majority of Paulley and Hughes' patients were 70–79 years. The mean duration of the illness in my patients was 7·1 years, while Ross Russell thought it exceptional for giant-cell arteritis to persist for 4 years, and in an early series Harrison [6] showed 7·2 months to be the mean duration.

Of my 50 patients, 10 have died. The causes of death were: purpura after gold injections, congestive heart-failure (2), pulmonary embolus, myocardial infarction, bronchopneumonia, miliary tuberculosis, chronic nephritis and uræmia, hæmolytic anæmia, and probable abdominal neoplasm.

6 of these patients had very detailed postmortem examinations but the most diligent search failed to reveal any evidence of active joint disease in the peripheral joints or spine apart from mild degenerative changes compatible with age. Prolonged search of other organs and muscles failed to show any evidence of rheumatic disease or arteritis.

10 muscle and other biopsies had been virtually normal. Perhaps the most conclusive evidence that the process is not comparable with the far more serious giant-cell arteritis is that 94% of my 50 patients experienced improvement and 30% became symptomless after an average period of 8 years' follow-up. All except 1 patient, who was tried on steroids, had salicylates only. Only 4% of the 50 continue to have considerable muscular discomfort up to now. Full details of this prolonged follow-up are being published.

Nuffield Department of Clinical Biochemistry, Radcliffe Infirmary, Oxford. L. BAGRATUNI.

SIR,—The interesting paper by Dr. Todd (Nov. 18) refers to the many names which have been attached to this condition by various recent "discoverers" of the syndrome. It was well recognised by the elder generation, and my chief, Sir William Willcox, taught that it was a variant of rheumatoid arthritis, which often manifests itself in this way in old people. He referred to it always as the "senile" type of rheumatoid arthritis, which he considered to be a relatively benign form of the disease.

I agree, therefore, with Dr. Todd in his conclusion that "it seems that the similarities (with rheumatoid arthritis) outweigh the differences, and that, in our present state of knowledge, this illness should be regarded as a rheumatoid variant". There seems little to be gained by not doing so.

London, W.1. W. S. C. COPEMAN.

THE INDUSTRY IT DESERVES?

SIR,—If the suggestion of Dr. Laurence (Nov. 4) that doctors should prescribe drugs by giving their generic name followed in brackets by the name of the manufacturer were generally accepted, this would put the clock back at least a generation to the 1920s and 1930s when this and similar systems of nomenclature were common.

In order to finance their research programmes, the companies in the pharmaceutical industry require strong brand identity and patent protection. For various reasons patent protection cannot be obtained for all the new drugs resulting from research, and strong brand identity is therefore of paramount importance to the manufacturer. I gather that those firms who have tried it find that the method suggested by Dr. Laurence does not provide adequate brand identity, which is why it has been largely abandoned. Its general adoption would certainly encourage copyists; but in a few years there might be little for them to copy as pharmaceutical manufacturers would no longer be able to afford the enormous cost of the research which goes into producing new drugs.

The Hinchcliffe report on the cost of prescribing had this to say (p. 79) about the problem:

"Firms should be encouraged to increase their research effort. Conditions which favour profits for research such as patent rights, the publicising of proprietary names, and the price agreement with the Ministry of Health should be accepted".

I am sure Dr. Laurence would agree that during the last 25 years the pharmaceutical industry has produced a vast therapeutic revolution with great resultant human and economic benefits, and that everything possible should be done to ensure that the contribution of the industry in the next 25 years is even greater than in the last.

It is admitted that a multiplicity of names for the same compound can be confusing to the practising clinician, but the existence of trade names in no way interferes with a doctor's right to prescribe drugs by their generic names if he wishes.

1. Cruz-Coke, R. *Lancet*, 1960, ii, 885.
2. Paulley, J. W., Hughes, J. P. *Brit. med. J.* 1960, ii, 1562.
3. Bagratuni, L. *Lancet*, 1956, ii, 996.
4. Bagratuni, L. University of Oxford D.M. thesis, 1958.
5. Ross Russell, R. W. *Quart. J. Med.* 1959, **28**, 471.
6. Harrison, C. V. *J. clin. Path.* 1947-48, **1**, 197.

That so many drugs are in fact prescribed by proprietary names implies that most doctors find these more convenient.

It is important to keep a sense of proportion about the drug bill. Last year the total cost of the pharmaceutical services was just over 1*d.* per person per day, and of this pharmaceutical manufacturers received rather more than ½*d.*

There is clear evidence that expenditure on drugs is self-financing in that it contributes more to the economy of the country than the drugs cost. For example, it has been estimated [1] that the economic contribution each year of the antituberculosis drugs alone is equal to manufacturers' sales of all drugs to the N.H.S.

Research expenditure by the pharmaceutical industry represents 12·5% of total N.H.S. sales, and the industry is currently investing another 15% in future development projects. If reductions in these expenditures are enforced, the future may be prejudiced.

Department of Clinical Investigation,
Parke, Davis & Company,
Hounslow, Middlesex. J. A. L. GORRINGE.

PRIMARY HYPERPARATHYROIDISM

SIR,—We agree with Professor Prunty (Nov. 4) and his colleagues that your editorial on this subject dismissed the phosphaturia of hyperparathyroidism too lightly. As they say, there are two major actions of parathormone which are clinically detectable, phosphaturia and hypercalcæmia; and so it seems reasonable to seek both these signs in suspected cases.

Since only an operation can confirm this diagnosis, clearly analyses of "proved" cases of hyperparathyroidism contrasted with "renal-stone" cases not explored, can reflect only the hospital's usual indications for operation, unless all the excluded cases have also been subjected to operation. Hypercalcæmia is the most traditional indication for the operation, and consequently few "proved" cases have not shown this feature; yet Professor Prunty and others have shown that this traditional sign need not be present. More important, typical cases show both features, and checking phosphate excretion can avoid parathyroid exploration in other types of hypercalcæmia. For example, Hodgkinson [2] found 80% of "proved" hyperparathyroidism to have both hypercalcæmia and phosphaturia, and 80% of his unoperated cases of non-hypercalcæmic "renal stone" showed no phosphaturia; we suspect that he might have had even closer agreement after a preliminary diet (see below). Probable cases without both features are not yet in urgent need of exploration.

But while the estimation of serum-calcium is a straightforward, although difficult estimation, there is no general agreement on how to test phosphaturia. It may be questioned whether the troublesome phosphorus-infusion procedure mentioned by Professor Prunty is needed for routine testing. There are various simpler methods for indexing phosphaturia which are reliable provided they can take account of the renal function and the blood-level—as in our phosphate excretion index.[3,4] An equally important point is the need to standardise the diet before measuring phosphaturia, since this clearly can influence any index of phosphaturia.[5] Thus, we feel that measurements of phosphaturia need a standard intake of phosphorus and calcium for some days beforehand, after which the simple collection of fasting blood and urine for a phosphate-excretion index is probably as valid as any, and certainly an important test to do in cases of suspected hyperparathyroidism.

Postgraduate Medical School,
London, W.12. R. FRASER.

1. Seale, J. R. *Brit. med. J.* Nov. 11, 1961, p. 1285.
2. Hodgkinson, A. *Clin. Sci.* 1961, **21**, 125.
3. Nordin, B. E. C., Fraser, R. *Lancet*, 1960, i, 947.
4. Nordin, B. E. C. Advances in Clinical Chemistry. Chicago, 1961.
5. Fraser, R. 1st International Congress of Endocrinology, Copenhagen, 1960.

THE CASUALTY DEPARTMENT

SIR,—I should like to join Mr. Lowden (Oct. 14) in admiring the report on the investigation by the Department of Health for Scotland into the Provision and Design of Casualty and Accident Departments.

I agree fully with his criticism of the recommendation to use a large number of small rooms, and I feel that the complex requirements could have been better answered than by this "easy solution".

The difficulties in the administration of a large number of anxious people and sometimes anxious personnel endorse para. 196 of the report, which emphasises the need for simplicity; but under these circumstances the organisation adopted must also be near foolproof, and there is a real danger of oversimplification. The cafeteria system and the separate-cubicle system are not mutually exclusive and both can be used to enhance the advantages of each.

I can also understand Mr. Lowden's scepticism about the use of clean and dirty theatres. Although we have much new information about the mode of infection by the staphylococcus, wound-exposure times and operation times in the casualty unit are short and contact and cross-infection play the biggest part in wound contamination—especially in the hubbub of the average department. Breakdowns in aseptic routines are numerous, and new loopholes make their appearance almost every day. Dr. Green (Oct. 21, p. 921) indicated this and emphasised the need to continue aseptic rituals or establish them before embarking on more specific anti-staphylococcal measures. The task of separating cases to maintain 100% asepsis in a clean casualty theatre is formidable but not impossible.

Over the past four years, two provincial casualty units, each with an attendance of 80–100 new patients daily, and with widely different clientele, accommodation, and supporting organisations, have been organised round the problem of preventing cross-infection. A primary separation of cases on the basis of infection has been made as follows:

(*a*) Up to eight-hour-old injuries are seen separately in cubicles. Wounds are kept covered, and explored and treated only in the "clean" theatre. Non-touch dressing and operation techniques are used throughout. 100% skin cover and occlusive dressings complete the protection.

(*b*) All known sepsis is segregated. Cases are seen in separate cubicles and daily septic clinics are arranged at off-peak periods.

(*c*) All other cases, comprising the bulk of work in the department. Appointments are given to return cases.

The division is simple in that the receptionist has only to assess whether there is frank sepsis and whether an injury is recent: "Have you an abscess?" "When did you injure yourself?" All other cases go into category (*c*). The reason for category (*c*) is that it is often impossible to decide whether there is infection or not until a case has been examined, and sometimes not even then. It allows a considerable margin of error for mistakes by the receptionist and subsequently, and, acting as a buffer between the clean and dirty side, prevents any accidental contamination of the clean theatre by "doubtful" cases. The fact that return wounds are either healed and free of the risk of infection or presumed infected is taken into account in organising category (*c*) on the cafeteria system. This system increases the speed at which patients are dealt with and does not necessarily introduce the undesirable features mentioned in the report.

The clean side thus rigidly protected from cross-infection forms a suitable environment in which to introduce recent trauma and in which anti-staphylococcal measures, such as disinfection of patient and staff, "pressure" ventilation, and possibly ultraviolet radiation, would hold a reasonable prospect of success.

Insufficient emphasis has been given to the extent

and effects of casualty-acquired sepsis in both inpatient and outpatient wounds, casualty-acquired sepsis as a cause of failure in later operations, and casualty-acquired sepsis as a source of serious outbreaks of ward sepsis. The problem of its control cannot be treated lightly and a simple division of patients into clean and infected does not offer a practical solution. The three-way division does guarantee asepsis in a " clean theatre ".

Although the organisation described has not been based primarily on the social requirements of the patient, or on works-study aimed at spoon-feeding him through the department, these are fundamental considerations and it is surprising how the various parts of the organisation interdigitate, allowing an easy flow of patients and work. It coordinates rather than complicates the confusion which results when an attempt is made to fit a great variety of patients and requirements into one system—cubicle or cafeteria.

Southampton. E. P. ABSON.

SIR,—I must pay tribute to the memorandum by Mr. Lamont, The Casualty Dilemma (Nov. 25). For years I have felt that the casualty department was the most vulnerable one in the hospital. Yet poor, defenceless, inexperienced men were automatically allotted to this department—a post which requires high judgment and ceaseless vigil—and even then, it is as Mr. Lamont says, carried on to the accompaniment of vulgar abuse. The remedy he advocates should be taken to heart by all hospital governors, and that right speedily.

Solihull, Warwickshire. E. S. PAGE.

HÆMOPHILIA A IN A GIRL

SIR,—Professor Steinberg (Oct. 14) suggested that the girl with hæmophilia, reported by us as a homozygote, would, in fact, be, heterozygote like the case recorded by himself and Dr. McGovern. It is, of course, impossible to know for certain whether our case is a homozygote or heterozygote. On the other hand, our patient differs from that of Steinberg and McGovern in more than one respect: in our case the hæmophilia is much more severe; in our patient the disease is as severe as in the affected males in the same family; and Steinberg's case may, in fact, be a male like the case described by Nilsson et al.[1]

Finnish Red Cross
Blood Transfusion Service,
Helsinki, Finland. H. R. NEVANLINNA.

PREVENTION OF PRESSURE SORES

SIR,—The article by Dr. Exton-Smith and Dr. Sherwin (Nov. 18) implies that 20% of patients newly admitted to a geriatric unit will develop a pressure sore. This curiously high incidence contrasts with my own experience which indicates between 8 and 12% as a figure closer to reality.

It may well be that our differences would be resolved on the basis of semantics, for no definition was attempted by your contributors. By my definition, a pressure sore entails the destruction of the full thickness of the skin, thereby exposing subcutaneous tissue, whether fascia, fat, muscle, bone, or other structure. I believe, too, that such a pressure sore arises ab initio from necrosis of subcutaneous tissue, which only later breaks through the skin after a dusky red erythema has appeared and subsequently sloughs.

It would be of interest to learn whether Dr. Exton-Smith and Dr. Sherwin included the very common superficial cutaneous abrasions among their " pressure sores ".

1. Nilsson, I. M., Bergman, S., Reitalu, J., Waldenström, J. *Lancet*, 1959, ii, 264.

I am not trying to discount the usefulness of their ingenious apparatus for recording the nocturnal spontaneous movements of patients in bed. If it is possible to distinguish those patients likely to develop a bedsore from those who are unlikely to do so, that will enable nurses to concentrate their attention on the selected group " at risk ", in whom bedsores would be effectively prevented by a rigorously applied regimen, involving turning the patient two-hourly by day *and by night*.

Cowley Road Hospital,
Oxford. P. D. BEDFORD.

TREATMENT OF MULTIPLE SCLEROSIS WITH CORTICOTROPHIN

SIR,—The study by Dr. Miller and his colleagues (Nov. 18) is a valuable contribution to a subject complicated by the variable course of multiple sclerosis and its liability to spontaneous remission. The only comparable controlled studies have been those of Alexander et al.[1,2] which they quote. The earliest observation by Jönsson, von Reiss, and Sahlgren,[3] and an impressive report by them on 51 treated patients [4] seem to have escaped attention, as do (pace!) my own observations.[5,6]

My series of corticotrophin-treated patients now totals nearly 70, and started in 1954. Most of these patients are on long-term maintenance treatment, and perhaps represent the largest group so treated over a period of years in this country. The following observations drawn from this experience may be of some use:

(1) Oral steroids are *not* as effective as corticotrophin in promoting remission of an acute episode, and are useless in doses that do not produce side-effects in preventing relapse or progression of the disease.

In disagreeing that corticotrophin and prednisone are " almost interchangeable in most branches of medicine ", I would point to the contrary experience in ulcerative colitis,[7] rheumatoid arthritis,[8] and some cases of rheumatic fever, disseminated lupus erythematosus, polyarteritis nodosa, and giant-cell arteritis,[9] as well as encephalitis, which they mention. The reasons for this are likely to be found in the range of steroids, other than cortisol, released by corticotrophin.

(2) A surprising amount of improvement may be achieved by corticotrophin many months after the onset of an episode, for, though the aim should be to treat patients as early as possible because of better results, new cases are often not referred till an attack has been active for several months, or even a year.

(3) Improvement of retrobulbar neuritis and diplopia begins within 2–3 days of starting treatment, and this is conspicuous both subjectively and objectively. The same is true of an ataxic gait, and subjective sensory impairment to waist level may recede to the feet within a week, and impaired bladder function may recover. I have not been impressed by any diminution of neurological signs of pyramidal-tract involvement once present, but nystagmus may lessen.

(4) Miller and his colleagues draw attention to the early relapse in some of their cases after withdrawal of the drug. It is this feature which, in my experience, points to the need for long-term treatment in two types of patient—those with frequent relapses and those with progressive deterioration. We have had two complete failures despite adequate corticotrophin dosage, but relapses have usually occurred when for a variety of reasons dosage has been reduced too far. The tragedy of these cases is that, though they respond to an increased dosage they are left with a greater residue of disability after each relapse. It is

1. Alexander, L., Berkley, A. W., Alexander, A. M. *J. Amer. med. Ass.* 1958, **166**, 1943.
2. Alexander, L., Berkley, A. W., Alexander, A. M. Multiple Sclerosis: Progress and Treatment. Springfield, Ill. 1961.
3. Jönsson, B., von Reiss, G., Sahlgren, E. *Nord. Med.* 1950, **43**, 380.
4. von Reiss, G., Sahlgren, E., Jönsson, B. *Acta psychiat. neurol. scand.* 1953, **28**, 429.
5. Paulley, J. W. *Brit. med. J.* 1957, i, 760.
6. Paulley, J. W. *ibid.* 1959, ii, 99.
7. Truelove, S. C., Witts, L. J. *ibid.* 1959, i, 387.
8. Savage, O., Denis, P., Chapman, L., Popert, A. J., Robertson, J. D., Copeman, W. S. C. *ibid.* 1951, ii, 1257.
9. Paulley, J. W. *ibid.* 1960, ii, 1562.

this that makes intermittent corticotrophin for each episode less attractive in these patients than long-term therapy aimed at amelioration or prevention of relapses.

I have found that for many patients the maintenance dose of about 10–15 I.U. gel every other day, which I advised in 1957, is too low. After 2–3 weeks' high initial dosage I now give 15–20 I.U. of the gel, or long-acting preparation, daily with potassium chloride. If one is in doubt of the efficacy of the dose, the 24-hour output of steroids in the urine may be estimated, but the patient's weight and appearance are usually a sufficient guide. To a stranger they should not look as if they were on corticotrophin, but it should be just apparent to the physician who first saw them; they should be kept a few pounds over their base-level weight.

Rarely 30 I.U. daily has been required to achieve the necessary adrenal response. One girl, after having very frequent episodes of retrobulbar neuritis over 2 years while on 20 I.U. daily, has had none for 18 months on 30 I.U. daily. No instances of pituitary suppression have yet been recognised, and as yet no vertebral collapse, though X-rays of the spine are advised from time to time.

The value of corticotrophin in acute episodes speaks for itself and now receives support from controlled series; whether the expense, inconvenience, and hazards of maintenance treatment will be justified by its benefits is a thornier problem, and one to which I have given some thought. Its solution depends on the assessment by unbiased observers of patients treated over not less than 5 years and their comparison with a comparable untreated group. Patients could also be used as their own controls using a relapse-rate index for a given period of time before and after treatment.

I conclude with a rather sad story. Two years ago the manufacturers prepared for me some inert gel to resemble corticotrophin gel. It seemed that to stop a treatment given for 2–3 years or more could not fail to carry psychological import to some patients. 3 patients were chosen for their exemplary response to treatment, minor degree of persistent disability, and freedom from relapse for some years; they were given the inert gel unknown to themselves but with their doctors' knowledge. 2 relapsed within 6 months; the 3rd remained well for nearly a year before the subterfuge was discontinued. With this experience, I cannot bring myself to pursue this venture into scientific evaluation any further (1 of the patients lost his job because of his relapse, which has left him considerably disabled). Others who, with justification, doubt the value of this treatment may, however, find inert preparations offer a method of determining its efficacy.

Ipswich. J. W. PAULLEY.

SIR,—We sympathise with Dr. Miller and his colleagues (Nov. 18) in their difficulties in organising valid controlled trials in this condition, but we fear that their conclusion of the value of corticotrophin (A.C.T.H.) in bringing about remissions is premature.

It is claimed that in this group of 40 patients with active disease the 22 trial cases and the 18 control cases were "generally comparable in . . . age . . . as well as in the proportion classified as showing initial episodes of multiple sclerosis . . ."

From the brief data reported this seems open to doubt: the mean age of the trial group was 32·3, and of the control group 37·4 years. The statistical factors adduced prove that this age-difference came about by chance. But can the authors convince us that five years are insignificant in the prognosis of this condition, or anything else?

More important still, 6 patients in the treated group were in an initial episode of multiple sclerosis but only 2 in the control group—a serious incomparability, since it is fairly generally agreed that almost all patients will recover from the first episode, whatever the treatment. Patients with "acute exacerbations during remission" will also tend to do well as a rule—and in this group also there were more cases in the corticotrophin than the control group (8 : 6). Combining these two groups with a very good, and a very fair, prognosis we obtain almost twice as many patients in the corticotrophin group (14 : 8) and would, therefore, have expected the corticotrophin group to have had almost twice the number of good results, regardless.

When we get to cases with a bad prognosis (i.e., with "acute deterioration of existing disability"), we find that there are more in the control than the trial series (10 : 8), thus biasing the outcome even further in favour of the corticotrophin cases.

When we carried out a controlled trial of intrathecal tuberculin on an equally small number of cases with this condition [1] we felt that we had to try and match up pairs of cases which resembled each other as closely as possible as regards sex, age, duration of illness, type of illness (relapsing-remitting, and chronic), number of episodes, and degree of disability at the time of trial. In order to get fairly satisfactory "matches" we had to draw on a pool of potential control cases eight times the size of the trial cases.

Furthermore, if one tries to compare the effect of treatment on "episodes" one should match comparable episodes (i.e., 2 cases with retrobulbar neuritis, or 2 with transverse cord lesions, since the prognosis of "episodes" in these two locations is quite different.

Of course we must agree that the difference in the two published groups is statistically significant, but unless Dr. Miller and his colleagues provide further details to controvert our criticism we must conclude that the difference is due to ill-assortment of the two groups—and not to corticotrophin, the value of which remains unproven. If we are right, we hope that Dr. Miller will continue the trial until greater numbers provide an unequivocal answer.

Maida Vale Hospital, London, W.9. R. E. KELLY
E. H. JELLINEK.

NIGHT-CALL SERVICES

SIR,—I am pleased that you have allowed space in your columns for a short letter which will inevitably provoke much discussion on the quality and desirability of the present night-call services.

When I first came to London I worked for one of these organisations and my comments on it are as follows:

1. The headquarters was poky and dirty with no facilities for resting, reading, or sleeping.

2. At almost every session I attended, I was the only British national and certainly the only one with any prior experience of general practice. My impression was that these two attributes were disdained by this particular organisation.

3. Payment for services rendered was delayed and invariably had to be requested.

4. The most scrappy information was given by the "control" when sent out on a call, or when telephoning in; without insisting on full details, only the surname and address of the patient were given. The age, sex, diagnosis, and degree of urgency of the case were not volunteered.

5. Elementary mistakes were made in addresses; occasionally even the postal district was wrong. There seemed to be no standard map with proper cross-references.

6. It seemed to me that the organisation was accepting more work than it could reasonably cope with; the area covered was too wide for the number of doctors available, particularly on the night sessions.

7. The principle of being paid so much per call provokes a scramble for areas adjacent to the control and is basically bad. On the other hand, being paid a set sum per session may work against the best interests of the doctor.

8. The bags provided by the service contained no morphine or pethidine, which are the basic drugs of general practice.

I must make it absolutely clear that I am not against these services as such; having spent almost a decade in

1. *Brit. med. J.* 1961, ii, 421.

general practice, for some of the time as a single-handed practitioner, I am only too aware of the need there is in general practice for occasionally shedding the load. It is obvious that some doctors are doing this to excess: in those areas served by these night-call people, there are those who are never available to their patients after evening surgery. These doctors pay for their free time, but are they any worse than those men, equally unavailable, who exploit their junior partners or assistants?

No doubt others will be able to suggest improvements to these call services but I merely set down my observations.

As adverse financial circumstances may force me to offer my services once again to one of these organisations, I must perforce sign myself

DIPLOMATE.

WORLD POPULATION

SIR,—Apropos of your leading article of Nov. 18, I have often thought that if the contraceptionists were really sincere, they would make a resolute effort to tackle the problem of human fertility at a deeper level than any apparently attempted so far, by aiming at the destruction of libido. Natural selection has after all produced sexless populations among those highly successful types the ants and the bees. What chance has done for insects in the past, surely psychosomatic engineering could do for the future of mankind, and if anyone were to claim that sexual emotion was good as an end in itself, let him be reminded that all the great love stories of the world are tragic. Hence we might envisage a double gain, to tranquillity as well as to security.

The excipient for the (presumably) hormone preparation might well be some item of universal consumption, such as bread or water, and those selected for eugenic breeding would pass through the circumstances of conception by A.I.D. in unruffled calm. The dominant minority would very likely opt to contract out of the prevailing system, but for the majority how much the best! Go to it, Sir Julian!

Health Department,
Darlington.

JOSEPH V. WALKER
Medical Officer of Health.

EMERGENCY RESUSCITATION

SIR,—The incidence of obstructed airway through the nose may affect the choice of technique for the expired-air method of artificial respiration. In a study of 3676 subjects examined for their ability to breathe through the nose, we found that 48 (1·3%) had nasal block.[1]

Of the subjects 980 were children, 17 (1·7%) of whom had nasal block. 82 were small children between 5 months and 6 years of age, of whom 2 (2·4%) showed nasal block, though most of the children had abundant nasal secretions.

To get an impression of nasal patency after submersion, the influence of water on the mucous membranes of the nose was investigated in 5 volunteers. Fresh water and 4% saline were used (seawater usually does not contain more than 3·5% saline). Fresh water was instilled to fill the nose and the nasopharyngeal cavity, then left for ten minutes in 4 subjects, and for five minutes in a 5th subject. All were placed supine with the head hanging over the end of the table. Afterwards we found that in none of the subjects was nasal patency changed, and rhinoscopy showed no signs of hyperæmia or œdema of the nasal mucous membranes. Next, the saline solution was instilled and left for five minutes in the nose and nasopharynx of 4 subjects. Rhinoscopy afterwards revealed no hyperæmia or œdema of the nasal mucosa. 3 of the 4 subjects had unaltered nasal respiration, but 1 had increased secretions as the result of this very irritating procedure, and one side of the nose became totally blocked, though the other side was unaffected. The block disappeared after half an hour when the secretions stopped.

Even if the incidence of nasal block varies in different conditions, total block must be relatively rare. Even after submersion, patency probably would in most cases not be altered significantly. Nasal block, therefore, need not be an objection to the mouth-to-*nose* technique, as a first-choice method for expired-air resuscitation.

The Finsen Institute,
Department of Anæsthesia,
Copenhagen.

HENNING RUBEN.

1. Ruben, H., Knudsen, E. J., Krarup, B., Ruben, A. *Ugeskr. Læg.* (in the press).

HALOTHANE

SIR,—Your leading article stated that the use of halothane "in operative obstetrics, where there is a risk of postpartum hæmorrhage, is dangerous". This opinion is not supported by experience here.

During the past thirty months, nitrous oxide and halothane mixtures have been used by three anæsthetists for approximately 250 cæsarean sections, 300 forceps deliveries, and 50 manual removals of placenta. The maintenance level of halothane has been in the region of 0·6% to 1·2%, which seems to be rather lower than that used in some of the series referred to in your leader. In no case has bleeding during or after anæsthesia been excessive, and there has been no maternal mortality.

When specifically questioned, one of the obstetricians expressed the opinion that hæmorrhage was slightly increased, compared with previous experience with other anæsthetics. The other noticed no difference.

It is interesting to note that one patient with inversion of the uterus, brought in by the flying-squad, was anæsthetised by me, using the same method. Uterine relaxation was insufficient to allow reduction. Administration of halothane, 4·5%, for several minutes was needed. Then complete relaxation followed and correction of the inversion was simple. Halothane was immediately withdrawn, and uterine tone returned rapidly. There was no question of excessive bleeding.

In the light of this experience, during which respiratory depression in the baby has never given rise to anxiety, I am convinced that halothane in reasonable concentration is a safe and very satisfactory agent in obstetric anæsthesia.

Paisley and District Maternity Unit,
Thornhill Maternity Hospital,
Johnstone,
Renfrewshire.

G. K. MCLELLAN.

SIR,—Your leading article of Nov. 18 does not mention a distressing side-effect of the drug—namely, the violent shivering which comes on during recovery in the majority of patients. This condition, for want of a better name, is known as "the halothane shakes" and more than once it has been reported by the nursing staff as an epileptic fit. As it may come on in the lift while the patient is being returned to bed, and is sometimes accompanied by laryngeal spasm with resultant cyanosis, it may cause considerable alarm.

After a recent hemicolectomy in a patient anæsthestised with halothane and oxygen alone, the condition persisted for 90 minutes and was not relieved by intravenous chlorpromazine. The patient burst his abdomen on the third postoperative day, and it is tempting to think that the two events were not entirely unrelated.

This complication has been scarcely mentioned in the literature, but Apivor [1] has given a good account of it. It has been suggested that it is due to intense vasodilation, but other anæsthetic drugs give rise to this condition without this side-effect. It would be interesting to ascertain the real cause of this complication and how it might be avoided.

London, W.1. MASSEY DAWKINS.

1. Apivor, D. *Anæsthesia*, 1960, **15**, 11.

DELAYED BUT SUCCESSFUL TREATMENT OF RUPTURED UTERUS

SIR,—A woman who had a ruptured uterus and a fœtus in the abdomen for over sixty hours survived and was cured of all the resulting complications.

A Mosotho woman of 38, living far in the mountains, went into labour about midday on Oct. 23, 1960. She was looked after by her mother. (She was para 6, the first being stillborn; the other five children were all delivered normally and were alive and well).

A very strong labour ensued and 16 hours later ceased suddenly before the baby was delivered. She was carried to the Mountain Dispensary at Semongkong where the Mosotho dispenser treated her with phenobarbitone tablets while he tried to arrange for an aeroplane to collect her from the nearby airstrip. Bad weather prevented the plane from fetching her for $2^1/_2$ days. At last, after $^1/_2$ hour's flight she was admitted to hospital in Maseru at 4.30 P.M. on Oct. 26. She was in extremis: her pulse was 160 and blood-pressure 80/0 mm. Hg. She was obviously anæmic and dehydrated. There was an easily palpable superficial fœtal head above the pubis. A diagnosis of ruptured uterus was made, she was given morphine (gr. 1/6) and atropine (gr. 1/100), intravenous plasma was set up, and she was taken to the theatre. Anæsthesia was induced with thiopentone and suxamethonium chloride and a cuffed endotracheal tube was passed, anæsthesia being maintained with nitrous oxide, oxygen, trichlorethylene, and gallamine ('Flaxedil').

A macerated male fœtus weighing about 8 lb. was found in the peritoneal cavity, and there was a very low rupture of the anterior lower uterine segment which extended into the broad ligament on the left side. There was gross bruising of the bladder and considerable peritonitis. The uterine muscle was infected and friable. A subtotal hysterectomy and bilateral salpingo-oopherectomy of the "smash-and-grab" variety was performed. Two pints of blood were given postoperatively, and streptomycin (1.g.) and procaine penicillin (2 ml.) were given twice daily. The bladder was drained continuously for five days with an ordinary catheter instead of a Foley's.

The patient's condition improved steadily and on the 6th postoperative day the hæmoglobin was 86% and doses of antibiotics were halved. Thereafter the wound became septic and broke down on the 11th day, and secondary suture was performed by using vertical mattress sutures and double dolly dressings. The sutures were removed 14 days later. Penicillin and streptomycin were stopped and chloramphenicol (250 mg. q.d.s.) was given for 16 days. 3 weeks after operation a further pint of blood raised the hæmoglobin to 90%.

By this time a vesicovaginal fistula had developed and failed to close despite reinstitution of continuous bladder drainage. Convalescence was further complicated by obstetric palsies (bilateral foot drop and gross wasting of leg muscles, worse on the left side), but these improved steadily over the weeks with massage and exercises and were finally cured.

8 weeks after operation she had an episode of subacute large-gut obstruction, fortunately relieved by enemas. 6 weeks later the vaginal sloughs had separated. Examination under anæsthesia showed that there were no vaginal strictures, but a midline vesicovaginal fistula was discovered just anterior to the cervix and admitting the tip of a finger easily. This was repaired two weeks later by freeing the bladder on the posterior edge of the fistula and bringing it up as a flap behind the anterior edge with interrupted mattress sutures of dermalon.

The freshened edges of the vaginal mucosa were approximated with interrupted sutures of dermalon. On removal of the sutures a very small fistula remained which was situated in the midline and admitted a probe easily.

A month later this fistula was repaired from side to side using the method described by Chassar Moir. This, unfortunately, sloughed and broke down leaving a slightly larger fistula which was repaired a month later using the original technique. This time the repair was successful and the patient was flown home to her family fully recovered, 7 months after admission.

At her original operation a bilateral salpingo-oophorectomy was performed because it was judged to be a quicker procedure than conserving the tubes and ovaries. The sole object of the operation was to save the patient's life.

It is our routine to drain the bladder after all badly obstructed labours for five days since we feel that the incidence of vesicovaginal fistula is thereby reduced. A Foley's catheter is never used because the bulb presses on that part of the bladder most likely to slough.

It is most unusual for patients who are malnourished, as this woman was, to survive a ruptured uterus of more than twelve hours' duration. We attribute her recovery to: modern anæsthesia; immediate operation combined with resuscitation (in our experience it is a waste of time to wait for the patient's condition to improve before operating as it so seldom does); the fact that there was no fierce hæmorrhage when the uterus ruptured; and the fact that the infecting organisms were obviously sensitive to the antibiotics given (this is one of the few distinct advantages of being relatively far from civilisation and its antibiotics and resistant organisms).

Our thanks are due to the Director of Health, Basutoland, for permission to publish this case.

Maseru, Basutoland.

D. G. STANDING
J. H. DALY BRISCOE.

TOLBUTAMIDE IN CIRRHOSIS OF THE LIVER

SIR,—I read with great interest the paper by Prof. Inder Singh and his colleagues.[1] It is surprising that tolbutamide should have been used in cirrhosis of the liver, for the following reasons:

(1) "Tolbutamide interferes with various enzyme systems in the liver. Tolbutamide should not be given to patients with liver damage." [2]

(2) Tolbutamide may prolong the action of barbiturates.[2] Since tolbutamide by itself has no hypnotic actions of its own, it acts by interfering with the detoxification mechanism at the liver. This is analogous to the action of SKF 525A.

(3) Tolbutamide apparently also interferes with the detoxification of alcohol. The enzyme systems concerned in the oxidation of alcohol are blocked in the same way as by T.E.T.D.

Your contributors state that tolbutamide increases the glycogen content of the liver and consequently may protect the liver from various types of injury. If the aim was to increase the glycogen content of the liver only, why not achieve the same result by injections of insulin and glucose instead of using a known hepatotoxic drug?

Department of Pharmacology, Medical College, Calicut, India.

K. SAMU IYER.

*** We showed Dr. Iyer's letter to Prof. Inder Singh and his reply follows.—ED. L.

SIR,—Tolbutamide does not appear in the latest list of drugs that may cause liver damage.[3] There is also considerable evidence that tolbutamide does not have any toxic effect even on the damaged liver. In fact, László et al.[4] have treated acute hepatitis with the drug and reported rapid decrease in serum-bilirubin and quicker recovery-time.

Before we started our work, we were aware of the interference in the detoxication of alcohol and barbiturates by tolbutamide. Occasional intolerance to alcohol was already described in the

1. Singh, I., Sehra, K. B., Bhargava, S. P. *Lancet*, 1961, i, 1144.
2. New and Non-official Drugs; p. 486. Philadelphia, 1958.
3. Beckman, H. Pharmacology; p. 312. London, 1961.
4. László, B., Bruckner, P., Görgey, E., Tóth, B. *Orv. Hetil.* 1959, **100**, 1411.

very early reports on the drug by Dolger.[5] So far, the only practical significance of these findings has been to tell sensitive patients to abstain from alcohol. However, patients who have ignored our advice have fared no worse; most of them have only overcome the intolerance. We are inclined to discriminate between the "scavenger" enzymes and others in the liver. Neither alcohol nor barbiturates per se had any place in our trial to worry about.

The concept of "liver protection" is not a clear one. Increase in liver glycogen itself may or may not be a factor, but that it may be an index of protective influences at work is highly probable. It is true insulin increases liver glycogen, but its non-diabetic use in liver diseases has not been encouraging. We were, therefore, in no mood to indulge in an unrewarding procedure. Wallenfels et al.[6] who investigated the activities of at least 22 enzymes in glycolysis, the hexose-monophosphate shunt, and the citric-acid cycle, found that the adaptive rise of these enzymes, which occurred in untreated diabetics, could be reversed both by insulin and by tolbutamide, but the augmented activity for hexokinase, fructose-6-phosphate-kinase, phosphotriose-isomerase, and the malic enzyme was specific only for tolbutamide.

Therefore, convenience and ease of administration apart, there was something more to look for in tolbutamide than in insulin. Our results more than justified our attempt.

New Delhi. INDER SINGH.

HOMELESS FAMILIES

SIR,—The 1957 Rent Act is an insult to the Welfare State. The B.B.C. television programmes are now constantly showing us poor families walking the streets with nowhere to go, because they have been evicted by their landlords, for no good reason.

These people with young children often pay and are willing to pay £5 a week for a wet, dirty room. They do not shirk paying their rents. They are thrown out because they have children. It is time that we, doctors, remonstrated with the Government over this social injustice. Doctors have a standing in the community; and if we brought pressure to bear on the Government, some form of effective rent control might return.

I have visited all parts of London and entered about 400 slum dwellings on visits. The state of the houses in which most of the lower classes live is a national disgrace.

I feel strongly about this, because I believe that doctors have more duty to the community than to prescribe medicine and write forms. We should show what philanthropists we would like to be, by fighting strongly for the weak.

London, N.W.6. ANTHONY HALL.

α-HYDROXYBUTYRIC DEHYDROGENASE IN THE DETECTION OF MYOCARDIAL INFARCTION

SIR,—Elliott and Wilkinson [7] found an increased serum-α-hydroxybutyric-dehydrogenase (H.B.D.) in myocardial infarction. Prompted by their findings, we are studying H.B.D. in diseases of the heart and skeletal muscle.

In myocardial infarction we have invariably found a big increase of this serum enzyme, lasting 10–15 days or more. The highest value was 1400 Wroblewski units (W.U.), 24–36 hours after the onset of pain. A moderate increase has been found in some cases of heart-failure. The normal range was 90–160 W.U. (mean 127 ± 19 per ml. of serum). We have also found increased H.B.D. in muscular dystrophy, chiefly in children; and the enzyme activity decreased after treatment with galanthamine ('Nivalin'), an alkaloid isolated from the snow-drop (*Galanthus nivalis*) which has an anticholinesterase activity and has been used in various neuromuscular disorders.

In 2 children with muscular dystrophy (both 8 years old), H.B.D. values were 1080 and 810 W.U., and both fell to 600 W.U. after treatment with nivalin. 2 other children were studied only after treatment, when the values were 320 and 400 W.U.

In 3 adults with muscular dystrophy H.B.D. levels were 250, 280, and 310 W.U. The second and third cases were treated with nivalin, and H.B.D. levels fell to 200 and 245 W.U. In a case of myasthenia the H.B.D. level was in the normal range (120 W.U.).

We feel these findings point to a further connection between the H.B.D. and muscular tissue.

Clinica Medica Generale dell'Universita, Palermo, Italy. LUIGI PAGLIARO ALBERTO NOTARBARTOLO.

5. Dolger, H. *Metabolism*, 1956, **5**, 946.
6. Wallenfels, K., Creutzfeldt, W., Summ, H. D. *Klin. Wschr.* 1957, **35**, 849.
7. Elliott, B. A., Wilkinson, J. H. *Lancet*, 1961, i, 698.

TRACHEOTOMY AND EMPHYSEMA

SIR,—From our experiences in the treatment of acute respiratory infections in emphysema, we should like to comment on the article by Dr. Harris and Dr. Houston (Nov. 25). We have treated thirteen such patients by tracheotomy and artificial ventilation with a Smith-Clarke respirator; only one patient died whilst on the respirator, and the rest recovered from their acute chest infections. Four patients died later (3 weeks to 18 months after their tracheotomy), but two of these deaths were not attributable to lung disease. Comparison of the few estimated arterial pCO_2 values given by Dr. Harris and Dr. Houston with our arterial pCO_2 measurements suggests that most of our patients were more seriously ill.

We agree that in many patients, with or without emphysema, aspiration of secretions via a tracheotomy tube may be lifesaving. But the common and major problem in emphysema arises when a gross derangement of both arterial oxygen and carbon-dioxide tension develops as a result of an infection which would probably be self-limiting in the patient without chronic lung disease. It is in some of these patients that artificial ventilation through a tracheotomy tube may be essential. From the data given by Dr. Harris and Dr. Houston, it seems to us very doubtful whether some of the patients did in fact have a significant degree of emphysema (cases 11 and 15). We cannot understand why case 12 became stuporose on 100% oxygen when his estimated arterial pCO_2 was 44 mm. Hg. What was the reason for this? It surely could not be carbon-dioxide narcosis unless the estimated pCO_2 was in error.

The value of early tracheotomy in some patients with an acute respiratory infection is undoubted, but the indications for assisted ventilation are much more difficult to assess. In our view measurement of both the arterial pCO_2 and pO_2 is essential for (1) correct diagnosis, (2) selection of the method of treatment, and (3) subsequent management. Unless data relating to both arterial gas tensions are given, it seems to us that doubts about diagnosis must remain and therapeutic conclusions may well be invalid.

Once artificial ventilation has been started the arterial pCO_2 is usually corrected rapidly, but this alone is a poor guide to the adequacy of ventilation. In this respect the pO_2 is the best variable to follow. In several of our cases a satisfactory arterial pO_2 was only maintained when the patient was ventilated with 100% oxygen. We suggest that 50–55% oxygen may be inadequate in many patients. We would add that ventilation with 20–25% oxygen may well result in cerebral anoxia; this is because artificial ventilation will lower the arterial pCO_2 effectively, and

hence reduce greatly the cerebral blood-flow, but it will not raise the arterial pO_2 adequately. One of our patients became unconscious on the ventilator as soon as 100% oxygen was no longer used to ventilate him, even though his arterial pCO_2 was quite normal.

Department of Medicine,
St. Thomas's Hospital
Medical School,
London, S.E.1

R. D. BRADLEY
D. S. C. CADMAN
S. J. G. SEMPLE.

CONVULSIVE EFFECTS OF TRANYLCYPROMINE AND IMIPRAMINE IN COMBINATION

SIR,—Recent clinical reports by Babiak [1] and Bateman [2] prompt us to draw attention to the convulsive electroencephalographic effects we have observed in laboratory animals treated with imipramine and tranylcypromine.

Tranylcypromine (' Parnate ') has been shown to produce immediate E.E.G. desynchronisation, similar in characteristics and intensity to that observed after giving amphetamine. In contrast, imipramine (' Tofranil ') tends to synchronise rather than desynchronise the E.E.G., and its E.E.G. effects are similar to those observed with the phenothiazines (chlorpromazine and trifluoperazine).

When these two compounds (imipramine 10 mg. per kg. and tranylcypromine 5 mg. per kg.) are given in combination, the E.E.G.-activating effects of tranylcypromine dominate the recording. If the animal is pretreated with imipramine (10 mg. per kg. per day) for 5 days or more, and is then given tranylcypromine (5 mg. per kg.), bursts of high-voltage activity are seen in the E.E.G. These soon give way to alternating periods of convulsive activity followed by periods of postictal depression and eventual death. Such abnormal E.E.G. effects are not observed if no imipramine has been given for at least 7 days before first giving tranylcypromine.

These observations are of particular interest in view of recent fatalities [1 3] following accidental and intentional use of these two drugs. It is clearly hazardous to give these compounds without allowing sufficient time for one drug to be completely eliminated from the body. The possible mechanisms of these convulsions remain to be clarified.

Our investigations were carried out under a Federal Mental Health Grant.

Department of Pharmacology,
Faculty of Medicine,
University of British Columbia,
Vancouver, Canada.

G. M. LING
M. NAGAI
S. HANSEN.

A NEW IRON LUNG

Dr. W. H. Kelleher writes:

" Although implied, it was not made clear in my article of Nov. 18 that the manufacturers of my new respirator were the Cape Engineering Company Limited, whose works are in Warwick, England."

DISTAVAL

Mr. D. J. Hayman, managing director of the Distillers Company (Biochemicals) Ltd., writes:

We have just received reports from two overseas sources possibly associating thalidomide (' Distaval ') with harmful effects on the fœtus in early pregnancy. Although the evidence on which these reports is based is circumstantial, and there have been no reports from Great Britain, either clinical or pharmacological, we feel that we have no alternative but to withdraw the drug from the market immediately pending further investigation. We are also withdrawing ' Valgis ', ' Valgraine ', ' Asmaval ', and ' Tensival ', all of which contain thalidomide. We will continue to carry out pharmacological and other studies of our own, and the medical profession will be kept fully informed of developments.

1. Babiak, W. *Canad. med. Ass. J.* 1961, **85**, 377.
2. Bateman, C. R. *ibid.* p. 959.
3. Robertson, D. S. *ibid.* p. 711.

Public Health

Routine Immunisation

THE evidence that immunisation against diphtheria with alum-precipitated toxoid (A.P.T.) slightly but definitely increased the risk of paralytic poliomyelitis led the Ministry of Health in 1957 to replace the issue of A.P.T. by that of formol toxoid (F.T.). For the same reason it frowned—but without severity—on the use of combined prophylactics for children. This September it issued to local authorities some suggestions on immunising procedure which amount to a right-about-face.[1]

There is some evidence that F.T. is not a satisfactory agent for primary immunisation; and poliomyelitis is at the moment a rare disease. Moreover, vaccination against poliomyelitis makes infection after other immunising procedures unlikely. Many local authorities are already using combinations of prophylactics against diphtheria, whooping-cough, and tetanus without obviously disastrous consequences. There may be theoretical advantages in single inoculations; but mothers do not care to have their infants treated as pin-cushions, and there is evidence that some combinations give no worse, and perhaps give better, immunity. For these reasons the Ministry recommended in September the use of a combined diphtheria-pertussis-tetanus prophylactic (three doses), Salk vaccine (three doses), and vaccination against smallpox—all in the first two years of life. Immunity against diphtheria, tetanus, and smallpox can be reinforced at school and B.C.G. given after the age of 12. Two alternative schedules are suggested. In schedule P whooping-cough vaccine (in combination with diphtheria and tetanus prophylactics) is given early in life, since fatalities from this disease are commonest in the first six months. The disadvantage of this schedule is the risk of paralytic poliomyelitis induced by two toxoids and a bacterial vaccine. Schedule Q begins with vaccination against poliomyelitis and defers immunisation against the other diseases until the age of six months or more, by which time antibody production nears its maximum. The responsibility for the choice and provision of prophylactics will in future lie with the local authorities.

These proposals were no doubt welcomed both by those who hold the needle and by the mothers of those who receive it. We hope that further attention will be given to the problem of marking permanently those who have been immunised against tetanus. A serum reaction is a cheap price to pay for avoiding that disease, but active immunisation is designed to prevent both these misfortunes. The Ministry made it clear that its circular was liable to modification; and already it has authorised routine use of attenuated-virus vaccine, administered by mouth, for immunisation against poliomyelitis.[2]

Among the questions most often asked of a medical officer of health are those concerning immunisation, and some of these are not easy to answer pat. As a comprehensive source of accurate information we know nothing better than the *Memorandum on Immunological Procedures*, now issued by the War Office in a new edition.[3] It is, of course, primarily concerned with the health of the soldier, but the needs of camp-followers of all ages receive attention. It lists those parts of the world where the traveller must be inoculated against yellow fever. It describes in detail the intradermal administration of T.A.B., which will be new to many and which must have saved a lot of discomfort. There are excellent descriptions of the various kinds of reaction which may follow immunisation and adequate directions for prevention and treatment. There are admirable suggestions for picking up the thread of an interrupted course of prophylaxis. There is a useful table of the expected life of immunising substances stored in the cold and at room temperature. It is, indeed, difficult to find a question which cannot be answered with the help of this very cheap book.

1. Ministry of Health: circular 26/61. See *Lancet*, Sept. 16, 1961, p. 653.
2. See *Lancet*, Nov. 4, 1961, p. 1021.
3. Memorandum on Immunological Procedures. W.O. Code 13161. H.M. Stationery Office, 1961. Pp. 79. 4*s*. 6*d*.

The medical officer of health or, for that matter, any family doctor who wants a reliable and up-to-date guide to practical immunology will do well to keep it on his desk.

Fish Out of Water

Unrewarded efforts to persuade a firm to improve the hygienic conditions of a fish shop are described by Dr. J. D. Kershaw, medical officer of Colchester, in his report for 1960.

In 1956 the public-health department had the strongest possible evidence that staphylococcal contamination of exposed fish, almost certainly by dust, had occurred and had caused at least one case of poisoning. The firm was approached; and next year Dr. Kershaw was assured that the shop was scheduled for conversion. In 1958 he learned that the firm was seeking an alternative site. In 1959 an interview with the firm's area manager produced no satisfactory response—the firm could not agree that fitting a glass window would effect any improvement, and it was not ready to go to the expense of installing refrigerated display cabinets in the existing premises. It did say that the matter might be solved in its modernisation programme, to be completed by the end of 1962.

This, says Dr. Kershaw, is an example of the way in which a large and wealthy national concern may sometimes view matters of food hygiene: smaller and less wealthy undertakings have had modern food display apparatus in use for years. The "little shop at the corner" is no more likely to be dangerous than the big store. Dr. Kershaw hopes that, before he retires from the authority's service in 1970, either the firm will have done something of its own accord or the Food Hygiene Regulations will have been strengthened so that his department can take stronger action.

Parliament

Community Workers

In moving the second reading of the Bill which is to set up training councils for health visitors and social workers,[1] Miss EDITH PITT said that these two groups had much in common—both worked in people's homes, both worked on their own though often in cooperation with others. It was therefore proposed that their training councils should have some members in common and the same chairman. Sir John Wolfenden had accepted this key position. Training for the health visiting service was long established, and the council would be able to make use of the high standards set by the Royal Society for the Promotion of Health and the Royal Sanitary Association of Scotland. On the other hand, training for social work in the local authority health and welfare services was new. It was hoped that workers with a university training would enter the local authority service, but the bulk of this work would fall to people with the new general training. At first the council would be concerned with social work in the health and welfare services, but the Bill did not limit its scope. It was hoped that local authorities would appoint some people to the council with experience of other services and thus facilitate, for example, eventual extension of the council's function to child care. The new councils would be financed by the Exchequer, and it was estimated that they would need about £50,000 annually.

The success of the services for prevention and for community care would largely depend on the work of these two training councils. Without the stimulus to training, many of the aims of earlier legislation would remain unrealised—for example, the Mental Health Acts with their reorientation of care for mental disorder towards care in the community. Though the Health Service Acts and the National Assistance Act had been passed more than ten years ago, their aims could not be fully achieved without this small measure.

1. See *Lancet*, Nov. 11, 1961, p. 1099.

Mr. KENNETH ROBINSON welcomed the Bill though he thought it belated. He wondered whether the functions of the social workers' training council might in time extend to the hospital service and include training for probation officers, prison welfare officers, or even officers of the National Assistance Board. The services for which training was being organised through the Bill were all seriously understaffed, yet the councils apparently had no concern with the selection or recruitment of students and no power to make central training grants. He thought it optimistic to rely on local authority grants. The financial provision made for the councils seemed to be grossly inadequate. The councils were given powers to carry out and assist in research, but the explanatory memorandum said "the additional expenditure . . . on research . . . will be very small". This seemed to be little more than a "perfunctory genuflexion" to an idea.

Dame IRENE WARD regretted that there was to be no training council for psychiatric workers and hospital almoners. She thought that the local authorities had too many representatives on the councils and the professions concerned too few.

Mr. KENNETH LEWIS thought it might have been better to discuss where coordination could take place in the health services before settling the channels of training. For instance, only when the Minister had decided whether he would extend the hospital maternity service or encourage women to have their babies at home, could we determine the kind of training to be given to the health visitor and the social worker. At the moment he believed that their training was too narrow. He, too, felt that more use should be made of part-time workers. It would be a good thing if we could change the Welfare State, in which the Government did everything, into the Welfare Community, in which people were prepared to help each other. He thought that we had not yet begun to explore the use of people's spare time in jobs to help their fellows. But Mrs. JUDITH HART argued that voluntary work could only supplement, and never take the place of, full-time professional work, and she reminded the House how few trained workers there still were, especially in the mental-health service.

Mr. LEO ABSE considered that the Bill dodged the "clamorous need to fill the yawning gaps in the social services". In some areas, like Wales, the social services were so primitive and so chronically short of trained workers that the new councils would find it well nigh impossible to find tutors for those who wished to take their courses.

Mr. ENOCH POWELL, the Minister of Health, said that the link proposed in the Bill between the training of the health visitor and the social worker was a compromise, but he hoped that it would ensure their present coordination and perhaps lead to an even closer relationship. The professional and educational representation, if taken together, commanded a majority in both councils. He made no apology that the local authorities were strongly represented, for they were statutorily responsible for the provision of the services. The Bill left it open for other aspects of social work to be brought under the councils, and it would be inconsistent for him at this point to say exactly which should be included and which excluded, but any accessions must be willing. Only an Order in Council, and not legislation, would be needed to adjust the membership of the Social Workers Training Council.

There was no provision in the Bill for direct Exchequer grants to those who would take the courses promoted by the councils. The making of grants for further education was a function of the local authorities. It would be wrong, certainly at this stage, for that function to be taken away from the local authorities and replaced by direct grants from the Exchequer. We should see how the normal machinery works before we considered whether it had to be displaced or reinforced.

On research, there was a genuine misunderstanding about the terms of the last paragraph of the explanatory memorandum. In the course of their work the local authorities and the central Government departments come into possession of an immense amount of material which could be made to yield valuable information. With comparatively little extra expenditure, if the power were there, as it was not at the moment, this information

could be tapped by the authorities themselves and by academic bodies. It was because a very small expenditure, for which the powers would be given for the first time in the Bill, could yield these results, that reference was made to these relatively small quantities; but there was no implication that there was any intention on the part of the Government to limit research or to be niggardly in their approach to research.

It would be a mistake to think that, because recruitment was not mentioned in the Bill, it was not part of the councils' functions. If by recruitment was meant seeking suitable people to take these courses, then recruitment was quite firmly within the duties of the councils. We should certainly for many years be anxious to get every suitable entrant that we could into these courses and into these professions. The Bill was only a means to an end. That end was not even the training and employment of increasing numbers of well-qualified and suitable workers. The end was to be able to treat, to help, and to support in the community all who could best be helped, treated, and supported there.

Private Members' Bills

Mr. F. JOHNSTON SMITH's bill to empower local authorities to provide meals and recreation for old people will be read a second time on Dec. 8. Mr. LEO ABSE is presenting a Bill to amend the law relating to homosexual offences, which will be read a second time on March 9.

QUESTION TIME

Profits per Prescription

Lord BALNIEL asked the Minister by what percentage the average net profit per prescription dispensed by chemists under the National Health Service exceeded the 1956 agreed figure in each year since 1956; and what was the estimated percentage figure for 1961 if no alteration had been made on Nov. 1 in the system of remuneration.—Mr. POWELL replied: The 1956 settlement was not in terms of an agreed net profit. On my estimates, the average net profit per prescription produced in 1956 by the settlement of that year was exceeded by 30% in 1957, 40% in 1958, 50% in 1959, 80% in 1960, and would have been exceeded by about 100% in 1961 if no alteration had been made.

Senior Registrars

Mr. ROBINSON asked the Minister what immediate proposals he had, following his acceptance of the Platt report and his discussions with the medical profession, to solve the problem of the time-expired senior registrars.—Mr. POWELL replied: The Joint Advisory Committees on Senior Registrars, which boards are to set up, will be asked as a first charge to review existing time-expired registrars in the light of the recommendations of the report.

Children in Mental Hospitals

Mr. N. N. DODDS asked the Minister if he was aware of the general concern aroused by the case of a 10-year-old girl, who, instead of being placed in a special school for maladjusted children, has for seven months been the only child in a mental hospital with 1200 mentally ill adults; and, in view of occurrences in the past of a similar character, where boys and girls have been detained with mentally ill adults, how many further cases there were of children being kept with adult patients in mental hospitals.—Mr. POWELL replied: I am aware of this case. At April 1 there were 202 mentally ill children under twelve in psychiatric beds and about 260 places in wards for mentally disturbed children under thirteen.

Children's Wards

During the last two years in England and Wales 75 schemes for 131 new or reconstructed wards for children have been approved by the Minister of Health, and 27 schemes for 44 wards are under consideration. 44 schemes make specific provision for mothers of children under five.

Manchester Royal Eye Hospital

Because of shortage of nursing staff, 35 beds in this hospital have been unoccupied. 10 were brought back into use recently.

Obituary

ROBERT STANDISH-WHITE

C.B.E., F.R.C.S.I.

Mr. Robert Standish-White was the doyen of surgery in Matabeleland, and he was one of the first to bring modern scientific surgical methods to Central Africa. He died in Bulawayo on Oct. 14 at the age of 73.

He was born in Dublin, and he was educated there at the Presbyterian College and the Royal College of Surgeons. Soon after qualifying in 1909 he took up an appointment as surgeon to the Livingstone Hospital, Northern Rhodesia. In 1912 he joined the trypanosomiasis research unit established by the Chartered Company and worked under Warrington Yorke in some of the remote parts of the Chartered Territory. In 1914 he joined the R.A.M.C. and served with the Northern Rhodesia Rifles. Later he became principal medical officer to Murray's Column, which fought Von Lettow Vorbeck's Forces in the campaign in East Africa and Northern Rhodesia. At the end of the war he spent a year of postgraduate study in London, and then settled in surgical practice in Bulawayo.

In 1940 he again volunteered for active service and was posted to the Middle East, but, while awaiting embarkation in Cape Town, he sustained a perforated duodenal ulcer. On his return to Bulawayo he took on almost singlehanded all the surgery for the Rhodesian air training group of the R.A.F., dealing not only with routine work but also with any casualties from night-flying training. He had been appointed O.B.E., for his services in the 1914-18 war, and in 1945 he was promoted C.B.E.

After retirement from practice in 1953 he still gave freely of his time to many voluntary organisations, such as the Red Cross and the blood-transfusion service. He was also honorary medical director to the King George VI Memorial Centre for Physically Handicapped Children, where he attended every day. He was a member of the Medical Council of Southern Rhodesia from 1928 to 1951 and was president from 1943 to 1951. In 1954 he was awarded the title of emeritus surgeon to the Bulawayo General Hospital

J. C. S. writes:

"Robert Standish-White was one of the wittiest men I have ever met, and his patients, with good reason, adored him. However busy he might be, he unfailingly saw his postoperative cases twice daily until they were discharged from hospital. I have seen him do a ward round as late as 10 P.M., waking up his patients as he went along, and leaving behind him gales of laughter as he said the appropriate thing to each in turn. It was a measure of his charm that not only did his patients not resent being awakened but they felt that they had been cheated of part of their essential therapy if he did not pay them his customary evening visit."

Mr. Standish-White is survived by his wife and three sons, one of whom is an orthopædic surgeon in Salisbury, Southern Rhodesia.

Dr. R. J. HAMER HODGES

B.W. writes:

"Jim Hodges was quiet, gentle and reserved in manner. But still waters ran deep. Behind his shyness was a dedicated scientific outlook, to which was allied accuracy of mind, and a remarkable capacity for taking pains. His patients were always thoroughly examined before operation, and he always managed to imbue them with his own quiet confidence. In the theatre he was calm, and always the complete master of his trade. In a crisis his serenity was an example for the surgeon to follow. The operation over, his care for the patient continued until all postoperative complications had been resolved."

Notes and News

ROYAL COLLEGE OF SURGEONS OF ENGLAND

AT the third provincial annual general meeting of the College, which was held in Sheffield on Nov. 25, Sir Howard Florey was admitted to the honorary fellowship. Sir Arthur Porritt, the president, presented the annual report and drew attention to the amount of research which was now in hand in the departments of the college. It had become clear that one further appointment was a vital necessity—that of a professor of surgery. Mr. Harold Edwards, in his report on the post-graduate training of surgeons, said that the teaching provided by the college had changed and it was now a true course of study of the basic sciences rather than a cram course for examinations. A panel headed by Sir Clement Price Thomas had been appointed to help young surgeons, especially from overseas, to secure suitable posts in approved hospitals.

Mr. Naunton Morgan reminded the college that, though the assets had risen steadily in the past decade, the deficit on the general revenue account had risen steeply. Trust funds for specific purposes had been a boon to the college, but a great need at the moment was for a sharp increase in the assets of the general fund to provide the college with the ordinary revenue it needed.

Fellows and members of the college had been welcomed to the city on the previous evening by the Lord Mayor at a dinner in the traditional home of Sheffield's industrial life, the Cutlers' Hall. They also had the opportunity of visiting the outpatient department which is the first stage of the new teaching hospital, where some examples of the work of Sheffield surgeons was seen in demonstrations and films.

PHYSICIANS' FORUM

ANOTHER of the valuable Scientific Meetings now held from time to time by the Royal College of Physicians of London took place at the college on Friday evening and Saturday morning last week, with Sir Robert Platt, P.R.C.P., in the chair. On these occasions the speakers are adjured to speak rather than read, and to confine themselves to fifteen minutes at most—with previous rehearsals.

The fifteen communications were very various. Dr. C. T. Dollery and Dr. P. Hugh-Jones spoke of ways of measuring ventilation and blood-flow in different parts of the lungs; Dr. R. D. H. Stewart had found four patients in whom long-continued phenindione therapy was apparently responsible for goitre; and Dr. A. S. Paterson and Dr. F. Bracchi described how a normal subject was conditioned so that a pain stimulus accelerated the heart, and how he was afterwards able to control the heart-rate at will. Prof. S. D. Elek gave reasons for full investigation of future cases of infection by the cytomegalic inclusion-body virus; Dr. G. R. Thompson reported that Hb-C confers protection against falciparum malaria and said that sickle-cell trait is not, as commonly thought, benign. Dr. G. R. Tudhope and Prof. G. M. Wilson had found that many patients with hypothyroidism have pernicious anæmia and that subclinical deficiency of vitamin B_{12} may persist over the years despite thyroid treatment—observations suggesting that there is a common factor tending to damage both thyroid gland and gastric mucosa. Dr. Paul Fourman spoke on the prevalence of unrecognised parathyroid insufficiency in patients who have had thyroidectomy, and Dr. R. W. Luxton discussed his series of cases of radiation nephritis (see p. 1221).

AN EDINBURGH APPEAL

AT the presidents' annual dinner of the Royal Medical Society on Nov. 23, Sir Derrick Dunlop launched an appeal for funds to rehouse and refurbish this ancient association of medical students. Recalling how it had been formed in 1734 by six young men who had been offered a body for dissection, he went on to describe how the society had since become "highly respectable and is now incorporated by Royal Charter". At its house in Melbourne Place the society offered its members a historical library, now inadequately housed with many valuable volumes in need of repair, and a dignified hall for debates and meetings. But the other rooms of the old building were shabby and cold. He compared the society to a "proud, intelligent, very active and beautiful old duchess who is, however, much impoverished and in consequence a trifle down at heel". Nowadays, student subscriptions were not enough to support the society's "commitments and pretensions". Modest funds were urgently needed to improve the fabric, furnishing, library, and heating of 7, Melbourne Place. Soon, too, the society would have to face the problem of finding new accommodation. The county council of Midlothian had already bought property on either side of the society and in due course the council could acquire the society's house by compulsory purchase. The development committee of the university were willing to reserve space on the so-called "island site" for a new and still autonomous building for the society. For this project considerable funds would be needed, and Sir Derrick launched a public appeal which he hoped past members of the society would support generously.

Donations may be sent to the hon. treasurer of the society, 7, Melbourne Place, Edinburgh.

VOLUNTARY EFFORT IN SOCIAL AID

AT the 73rd Annual Meeting of the Invalid Children's Aid Association held in London on Nov. 21, Dr. A. White Franklin said that one of the most important developments of recent years is the proposed five-year trial of a case-work unit in London. The Invalid Children's Aid Association, the Family Welfare Association, and the Family Service Units are preparing a detailed plan, under which family case-work can be done from one centre. Such a scheme should bring about a better service and will show whether the workers' time and skill can be deployed to better advantage. The trustees of the London Parochial Charities have earmarked £60,000 to be spread over five years for the establishment of the unit.

Mr. Franklin also said that a home is to be set up for the care of non-communicating children, to try to get them back into the normal educational stream. This will cooperate with Dr. Louis Minski's diagnostic unit at Belmont. The Buttle Trust has given a generous grant, and the Banstead Boys' Surgical Residential Open-air School is being transferred by its trustees to the Association for this use. The Association is planning a conference on development dyslexia (word-blindness) early next year.

In an address on Social Work in the 1960s, Mr. George Haynes, director of the National Council of Social Service, said that originally the Charity Organisation Society, which brought the Invalid Children's Aid Association into being, had tried to find rules or lines of thought that would help citizens to help each other: the alternative of everyone doing his best was not good enough. What was needed eighty years ago was a better relation between the home and those caring for the children, to be produced by personal contact and home visiting. Today, facilities and amenities existed far beyond any hope of the founders of the voluntary societies; yet the illegitimacy-rate was extremely high, and there was some fear lest the present difficulties of the homeless in London might become such a flood that the problems facing the founders would return. New forces were always playing on society, and man had an indisposition to behave rationally either as an individual or in his social groups. The need for social work remained, though it must and would take different forms.

Under present legislation the mentally sick were more and more to be cared for within the community, but the question arose whether the community and the authorities were qualified to provide community care. In social work good will was not enough, and there was a need to understand problems more deeply and to apply help with trained skill. Eighty years ago all were volunteers, whose good will was not matched by ability to carry out the job on a regular basis; but Mr. Haynes thought that there were now volunteers who were prepared to work in the same way as professionals. The Invalid Children's Aid Association should think carefully how

such people could be collected, recruited, and trained, seeing that there were not enough professional workers.

In conclusion Mr. Haynes emphasised the need for the voluntary societies to follow their historical task of being socially inventive.

RESEARCH IN PSYCHIATRY

THE report for 1960-61 of the Mental Health Research Fund tells of continued expansion. 50% more applications for grants were received, and some £30,000 was committed to the support of twenty new research awards. The fund is the only institution concerned solely with research into mental health. Although primarily concerned with research, it has lately started to publish a series of pamphlets on the major mental disorders, to inform the public and to help to change its attitude towards psychiatric patients and research. Demand has been very great for the first pamphlet, *Schizophrenia*.[1]

Speaking at the annual general meeting in London on Nov. 20, Mr. I. T. Henderson, the chairman, said that the Fund had not made the progress it had hoped for in respect of permanent career posts in research. Mr. Henderson declared: "We have come across cases where first-class research workers have been lost to the field because of lack of permanent posts to which they might aspire." He regretted that, while many Governmental and other bodies had an interest in mental-health research, none was responsible for examining the problem as a whole.

L'HÔPITAL COCHIN

L'Hôpital Cochin, a large new hospital for the treatment of accident cases, was opened in Paris in 1959. It is associated with a general hospital and calls upon to its varied medical and surgical resources. *Le centre de traumatologie* is part of the orthopædic and rehabilitation service, and its objects are to provide an emergency centre, a burns clinic, a unit for acute sepsis, a teaching faculty, and an establishment for research into the problems of accident surgery. Funds to provide and house these facilities come from various sources—the *Sécurité Sociale*, the *Santé Publique*, the municipal authority, and the national department for education. A bulletin we have received illustrates the generous style in which the original idea has been executed; and there may be a lesson not only in the fact that Paris has paid such practical attention to accidents but also in the unity of the various authorities which has produced the money for it.

FILMS ON CHILD NEUROLOGY AND CEREBRAL PALSY

THE third edition of the National Spastics Society's film catalogue is being distributed as a free supplement with the December edition of *Cerebral Palsy Bulletin*. It is also obtainable, price 5*s*. or one dollar, from the National Spastics Society, 12, Park Crescent, London, W.1.

In the new edition the type and the paper have been improved and the catalogue is bound in the glossy brick-red cover now widely associated with the National Spastics Society's medical publications. Of greater significance is the change in title, which has been broadened to include child neurology. This edition of the catalogue contains details of 67 films, 13 of them produced since 1959, of which 4 are diagnostic films, 6 illustrate treatment methods or centres for treatment, and 3 are of general interest or have been produced for money-raising purposes. In addition, 10 titles have been included from the catalogue of the International Rehabilitation Film Library.

It is a pity that recent additions have been described more briefly, without the appraisals which were a valuable feature of previous editions. But the catalogue is an excellent publication, and this time it contains not only details of films but also two articles by Frank Bamping, who for some years was information officer of the Scientific Film Association. He writes from practical experience on the Organisation of Film Shows, and with great authority on the Movement of Films between Countries.

1. Obtainable without charge from the Fund, 39, Queen Anne Street, London, W.1.

TRANSFUSION EQUIPMENT

A NEW British standard for transfusion equipment has been drafted by a technical committee of the British Standards Institution, under the chairmanship of Dr. G. H. Tovey.[1]

The standard has been prepared to meet the needs of the National Health Service and the Armed Forces. In order to achieve interchangeability of components with those used in other countries, requirements have been specified as far as possible in accordance with proposals that are under consideration by a technical committee of the International Organisation for Standardisation.

The revised standard includes requirements for disposable giving-sets intended for single use and for equipment for taking blood. For certain items—including the closure, the drip-counter, and the filter-chamber—performance characteristics have been specified, but, in order not to restrict development, the design has not been specified in detail. Although the specification gives requirements for a suspension recess in the bottle, other means of suspension can be employed.

1. Draft British Standard Specification for Transfusion Equipment for Medical Use (revision of B.S. 2463): AB (SGC) 7832. Comments should be submitted by Jan. 5 to the British Standards Institution, 2, Park Street, London, W.1.

University of London

Dr. F. W. O'Grady, lecturer at the Middlesex Hospital Medical School, has been appointed to the readership in bacteriology at St. Bartholomew's Hospital Medical College. The title of reader in surgery has been conferred on Mr. J. C. Murray in respect of his post at King's College Hospital Medical School.

The following have passed the final examination for the M.B., B.S.:

Honours.—E. Q. Archampong (*a*,*c*), University College; C. G. Barnes (*e*), London; A. C. Buck (*e*), St. Mary's; Ann G. Creighton (*d*), Guy's; Barbara A. Etheridge (*e*), Middlesex; D. P. Goodwin (*d*), St. Mary's; Muhammad Muazzam Ilahi (*b*), Guy's; R. J. M. Irvine (*c*), St. Bartholomew's; Vanessa M. Jones (*d*), St. Bartholomew's; Elizabeth M. Knott (*e*), University College; J. W. Paterson (*c*), Westminster; B. D. Ross (*b*), University College; D. W. Straughan (*a*), Westminster; J. D. Ward (*b*), London; B. P. Whitney (*d*), Westminster.

(*a*) distinguished in pathology; (*b*) distinguished in medicine; (*c*) distinguished in applied pharmacology and therapeutics; (*d*) distinguished in surgery; (*e*) distinguished in obstetrics and gynæcology.

Pass.—K. W. Abel, D. E. Alder, D. A. Alderton, Solange M. M. Amos, T. M. Andrews, B. D. Apthorp, Antonia F. Bagshawe, M. R. Baldwin, R. N. Bale, P. I. Banky, J. P. Barker, A. N. Barnardo, M. J. Barnes, D. M. Barrow, M. T. Barton, S. M. Bass, Nirmal Singh Bilkhu, P. G. Bischitz, M. E. Blacklee, A. G. Boohene, G. T. Bowra, A. P. Bray, T. G. J. Brightmore, S. S. Brook, J. K. Brown, M. D. Brown, Rose Buchanan, R. E. Burfoot, Tibor Buzady, J. H. Chamberlain, Malcolm Chan, J. R. A. Chawner, Sally A. Cherry, Rosalind E. A. Chinnock-Jones, M. J. E. Chorley, P. B. Christian, Erpys Christopher, Winifred E. Cobbold, T. E. Cochran, J. A. Coden, J. S. H. Cohen, Rupert Collingwood, G. E. Conn, I. L. Craft, J. C. Crawhall, A. J. Crompton, J. J. L. Crosby, D. E. B. Davies, J. G. Davies, R. R. Davies, Sarah E. B. Davies, A. J. G. Davis, Carolyn J. Deeks, A. W. Diamond, R. H. Ellis, J. D. R. Evans, C. S. Flowers, G. H. Forman, D. R. Forsdyke, J. D. Fox, G. M. Froggatt, K. G. E. Frohnsdorff, A. M. Gallop, Michael George, Susan E. Gooda, A. D. G. Gordon, R. M. Greenwood, O. H. B. Gyde, M. G. Halford, D. L. Hall, Robert Hall, Jennifer M. Handley, Joseph Harris, C. T. Hart, J. E. Haselden, J. E. Hayes, M. J. Henry, Daphne M. Herbert, M. W. Hewson, V. J. M. Hickman, R. A. Hobdell, H. T. Hodnett, C. A. Hood, J. D. Hookway, Gillian R. Hudson, C. J. Hughes, D. M. E. Hughes, Gwilym Hughes, C. J. Hull, Shirley D. Hunter, Elizabeth A. Hutchinson, Christina M. Jenkinson, N. E. Jensen, B. R. Jewell, Rodney Johnson, J. H. Jones, J. R. L. Jones, M. C. Jones, N. O. Jones, A. G. Karseras, E. P. Kirk, N. J. Knight, Loretta Suet Wan Ko, Asif Hassan Ismail Lalljee, J. P. Leff, J. M. Leigh, P. D. Lewis, D. E. Lieber, C. D. R. Lightowler, A. J. Lopianowski, J. O. McFarlane, A. F. McGibbon, James McLauchlan, C. A. McNeill, H. N. Magnani, R. T. Maguire, J. E. Mandeville, A. J. Marengo-Rowe, R. T. H. Marsden, Valerie M. Marvin, A. E. B. Matthews, H. R. Matthews, A. H. Melhuish, A. D. Metten, A. J. Miller, Doreen M. Miller, Barrie Milroy, S. T. Minto, R. R. N. Molineux, Elspeth A. Morrison, P. J. Mullin, M. J. B. Nicholson, Rosemary R. Norton, J. E. Oliver, Gillian M. Oxenham, W. H. Pagan, R. M. Palmer, R. G. Palmer, P. W. McL. Parker, Elizabeth F. H. Parry, D. McC. Paterson, P. B. Pattison, B. J. D. Peatfield, J. E. Peck, R. L. Pell, C. J. Percival, D. A. Persoff, D. W. Pierce, Penelope J. Pollard, Ann R. T. Pomerance, C. A. Porter, Angela M. Powell, D. L. Powell, B. J. Preston, Eleanor P. Price-Jones, D. I. Prosser, J. P. Pryor, G. P. Rabey, B. J. Radford H. P. Rang, D. C. Reader, D. E. Rees, Daphne P. Richards, R. G. Richer, J. M. Robertson, Manijeh Sadr, P. R. Salmon, R. H. Salter, C. N. Scott, Gillian Scott, J. G. Scott, G. N. Shephard, Avril M. Sillitoe, Michael Silver, Jennifer E. J. Simmonds, Ann M. Sinclair, Akbal Singh, L. H. Smaje, C. R. Smith, D. T. M. Smith, Sheila K. Smith, Margaret E. Stafford, M. D. Steyn, C. A. Stossel, Glenda K. Swindells, Mary E. Tate, D. M. A. Taylor, J. M. Thistlewood, D. R. Thomas, L. R. Thomas, Brenda M. Thompson, C. J. Toynton, A. M. Tucker, J. McJ. Turnbull, A. J. Tyack, M. F. Tyrrell, R. C. Uren, J. H. Visick, D. A. Vissenga, R. C. Wales, W. A. Wallbank, Barbara Walsh, Jillian M. Wandless, Adrianne Watkins, J. R. Weatherill, Sheila M. J. Webb, D. G. Wells, Ann M. Whitehead, K. G. D. Williams, A. G. Wilson, P. J. Winter, Francis Kang Wong, S. M. Woolf, D. J. M. Wright, Jane E. Yeo, L. J. F. Youlten, Michael Young.

University of Aberdeen

Dr. R. E. Mackie has been appointed to a lectureship in mental health.

University of Edinburgh

Mr. W. McD. McQuillon has been appointed lecturer in orthopædic surgery and Dr. Hugh Miller lecturer in public health and social medicine.

Royal College of Surgeons in Ireland

On Nov. 17 the fellowship was conferred on A. P. T. Clery, P. J. Logan, and C. J. Mulvihill.

Royal College of Obstetricians and Gynæcologists

At a meeting of council on Nov. 25, with Mr. Arthur C. H. Bell, the president, in the chair, Dr. Sreemanta K. Banerjea was appointed William Blair-Bell lecturer for 1962. The following were admitted to the membership:

Shyamoli Datta Choudhury, Pilloo Khodayer Irani, Wai-Chee Li.

The following have been awarded the D.Obst.:

J. L. S. Alexander, W. W. Alderman, C. L. C. Arnold, R. M. Badminton, K. R. Ball, P. R. Bambridge, D. S. Bamford, E. E. Barnard, E. J. Barnett, A. M. Barnie-Adshead, Rachel M. Bartlett, Himansu Kumar Basu, Cyril Bate, Paul Beavon, J. M. Beeley, D. P. Beirne, A. D. Bell, C. F. N. Bennett, J. A. G. Benson, G. C. Bentley, E. H. Berman, Alan Bertram, Balideo Bisseru, Zarina Tayebji Biviji, J. H. A. Black, A. G. Bond, Helen D. Bower, K. R. Bowles, Elizabeth M. W. Bradford, J. T. Breen, J. R. Brew, C. C. L. Brewer, T. R. C. Brodie, P. P. Broughton, C. L. Brown, C. M. Brown, Joan M. Brown, R. M. Brown, Anne N. Bruce, T. B. Buchanan, A. L. Buckley, P. F. J. Bunting, D. R. Burcombe, G. M. Burke, J. C. Burn, N. B. Byatt, A. B. Byles, J. M. Cairns, Catherine D. Campbell, P. C. S. Chapman, Wilfred Obi Chukudebelu, R. B. Church, F. R. Cianchi, Gillian A. Clarance, Heather G. M. Clarke, R. J. Clement, Shirish Vaikunthal Clerk, Ian Cliffe, J. A. D. Clinch, G. B. Clinton Jones, Diana E. Clough, J. G. Cochrane, P. G. Coffey, M. A. Cole, M. D. Constable, Daphne I. Cook, F. G. Cooper, Sheila A. Corrin, C. McK. Corser, D. R. Couchman, A. J. Cox, Patricia L. Crawford, M. J. Critchley, David Crookenden, W. A. M. Cutting, J. A. Dacre, Sayda Dardiry, J. T. Dawson, J. G. Deller, Ansuya Mohanlal Desai, M. E. Dewar, Girija Dhar, Hugh Dinnick, R. X. Dixon, P. R. C. Dowse, Charmaine M. D'Souza, A. M. Duthie, Madan Mohan Dutta, D. J. Y. Dyer, N. C. Eccles, J. S. Edmondson, D. G. Evans, V. C. Faber, Rosemary Fairweather, C. G. Falkner, Davnet A. V. Fenton, Cecilia Fernandes, R. F. M. Forward, H. B. Francis, A. G. Fraser, R. M. Fredman, Frances E. Freeman, D. S. Freestone, D. L. Froggatt, David Galliford, J. S. Garvin, Asha Gauba, Elizabeth A. Gaze, Sughir Ranjan Ghosh, Iqbal Ghulam-Mohammad, Marjorie P. Gibson, W. H. Gibson, M. J. Gilbert, Gordon Gillespie, T. G. Girdwood, S. T. Godwin, Jeremy Goodchild, H. K. Gooding, Norman Gordon, G. J. K. Greenlaw, A. W. Grogono, B. H. Grundy, Rashda Maryam Hamid, K. W. Hancock, C. E. Harley, D. G. Harries, Evelyn W. S. Harris, P. W. R. Harris, B. A. Hasenson, M. J. Haugh, J. N. Haworth, R. J. Haythornthwaite, A. J. Hayward, G. N. Henderson, Ann Henley, Jinatissa Herat, Elizabeth M. Higham, Brian Hill, D. I. D. Hodge, Pauline Hollier, Rita J. Hornik, C. E. Horsfall, Ismail Hosny, Judith A. Houghton, P. J. C. Howe, H. V. Hughes, F. M. Hull, I. A. Hunter, R. F. Hurding, W. R. Hutton, M. T. Inman, M. C. H. Jackson, Edna M. Jacoby, J. R. James, W. H. M. Jewell, R. W. John, Lewis Johnman, H. H. G. Jones, J. H. Jones, Kanta Kanwar, Moira B. Kelly, P. W. Kershaw, Alan Kirby, G. P. Kirkland, Gool Ardeshir Kohiyar, H. M. Kohler, Jill E. Lakins, J. W. Latham, M. P. G. Lawler, Raymund Layton, R. A. Lee, Hoei Tjiang Lim, Therese Shook Chin Lim, Nancy G. Lord, I. S. Lees Loudon, D. B. Lloyd, Pramila Loghani, A. J. B. Luke, Elisabeth M. Lurring, Robin Lush, I. I. Macaulay, A. R. McCutcheon, P. T. MacDonnell, Helen P. McEwan, D. B. McFarlane, Terence McGovern, P. J. McGregor, Ruaraidh Wishart McIntyre, A. W. McKenzie, C. A. T. McKinney, Marjory G. McK. McKinnon, Eliza McLaughlin, A. C. MacLean, J. D. McLean, M. J. MacLean, H. D. MacLeod, A. L. Macnair, J. G. Madden, Mrinalini Malakar, K. C. Marwick, Anita Mascarenhas, Ramani Mathuranayagam, Florence Maung Maung, T. C. Mayer, J. A. Mead, Virbala Vijay Mehta, D. S. Meldrum, M. J. Mellor, W. P. Metcalfe, G. T. Millar, Janette Millar, Nityananda Misra, Marie H. H. Mitchell, Michael Modell, Noel Omar Mohammed, John Monkman, C. J. Morgan, R. H. Morgan, J. R. Morton, P. D. Moylan, J. T. Mucklow, Pushpa Mullick, Ronald Mulroy, William Murdoch, Michael Myers, Belinda J. Myles, T. G. Nash, J. P. Neasham, J. E. Noakes, D. L. Norris, Samuel Sonny Oghanna Nwosu, J. C. Oakley, Sean O'Connell, Barbara E. P. Ogden, M. J. Olver, Ma Nan Oo, M. J. Orrell, Kandappar Subrananian Padmanathan, Rosemary F. McL. Page, Sudha Ramanlal Parikh, D. S. Park, Ishwarbhai Bechardas Patel, Bhalchandra Bhaskarrao Patil, Margaret E. Pawson, Belinda Perry, J. R. Perry, E. N. Pickering, I. C. Pitter, Mehar Jabin Rashid, Hazel M. Rawlinson, Parial Shah Razvi, A. F. Richards, D. F. Richards, Julian Rivers-Kirby, Anne P. Roberts, E. G. Robertson, I. E. W. Robertson, Manjula Rohatgi, C. J. Rowland, D. A. W. Sansome, J. S. Seaton, P. R. Seed, Batul Mohesh Shah, Shantilal Vadilal Shah, Ronald Shapiro, L. A. Sherski, B. A. Sides, Shirley K. M. Sinclair, A. G. Slark, J. D. G. Sloss, M. G. Smedley, A. G. L. Smith, G. C. Smith, Margaret H. Smith, N. H. Smith, A. R. Snead, R. B. Somerset, Patricia M. Sonksen, Ian Soutar, Joanna South, P. G. Soutter, J. N. Stenhouse, Hilary Stirland, R. A. Stroud, A. G. Strube, J. C. Swann, W. M. Tait, Pauline E. Tan, Colette Taylor, J. P. Telling, D. F. E. Thallon, A. J. Thomas, Edith P. Thomas, E. H. Thomas, I. C. Thomson, Shail Kumari Tiwari, F. E. Tomlinson, Patricia A. M. Tootill, Stephen D. Turner, Anne M. Urquhart, Tara Hari Vanarase, Bik-May Wai, Joan M. Wallace, J. B. Warren, W. R. Watkins, Norah Webb, D. P. Wells, Paul Wentworth, Myra Wharf, J. E. White, R. G. White, E. I. Williams, M. K. Williams, Fenwick Wills, A. M. Wilson, M. A. Wilson, R. B. Wilson, P. J. Wise, R. A. Wiseman, Cheong Fat Paul Wong, I. H. Y. Wood, R. J. Woodhouse, D. G. Wray.

Bureau of Hygiene and Tropical Diseases

Dr. F. I. C. Apted has been appointed assistant director of the Bureau. Dr. Apted served from 1941 to 1951 in Sierra Leone and afterwards as sleeping sickness specialist in Tanganyika. He was a member of the editorial panel of the *East African Medical Journal* from 1960.

College of General Practitioners

At the annual general meeting held in London on Nov. 25, Dr. G. F. Abercrombie was unanimously re-elected president for 1961–62, and members of council for 1961–62 were appointed. About 200 members and associates were present.

The Foundation Council award was presented to Dr. W. N. Pickles. Dr. Eric Townsend was presented with the Butterworth gold medal for 1960-61 for his essay on Future Trends in General Practice, and Dr. J. A. Pridham received the second prize. Sixteen Upjohn travelling fellowships (up to £200 each) were awarded and Public Welfare Foundation prizes (£40 each) were presented to six final-year medical students.

Dr. Annis Gillie, chairman of council, reported that nearly £400,000 had been received or promised towards the college's appeal. The work of the 36 faculties had been energetic and enterprising, and an increasing number of general-practitioner symposia were being arranged each year. A research foundation of the college had been formed with Sir Harry Jephcott as chairman of its board and Dr. E. V. Kuenssberg as hon. secretary.

The terms of reference of this board are "to encourage general-practitioner research" in all its stages, especially that which cannot be carried out easily in a laboratory or hospital, or is confined to general practice. It is anxious to receive applications about research projects, particularly in their early stages.

During the year, said Dr. Gillie, the research committee of council had been more vigorous than ever. Two major studies—on diabetes (under the direction of Dr. D. L. Crombie) and on chronic bronchitis (under Dr. John Fry)—had been completed. The activities of the epidemic observation unit had been expanded. The college's register of congenital abnormalities was the largest and most comprehensive in existence, and the research register had proved very valuable.

After a debate in which 35 members and associates took part, the following resolution was passed by 126 members' votes to 15:

"That an examination in general practice be introduced as one of the criteria to be taken into account by the board of censors in considering applicants' requests for admission to membership of the college."

An announcement about this examination will be made later. It will not be held next year.

Annual Dinner

At a dinner at Apothecaries Hall on Nov. 24, the toast of The College was proposed by Mr. Enoch Powell, Minister of Health.

Drawing a parallel between the work of the member of Parliament and the work of the general practitioner, he pointed out that the two have much the same clients—the one who comes in just for a chat; the one who comes to air the same old grievance; the one who needs reassurance ("and you'd be surprised what a nice little psychiatric practice builds up over the years"); the one who comes too late; and the one for whom something can actually be done. These were the same types because they were the same people—seen, as the general practitioner sees them, as human beings in their family environment. Nowadays, said Mr. Powell, wherever one goes there seems to be a committee considering what is the function of general practice. With Dr. Annis Gillie as chairman, a committee of the Central Health Services Council is to report on the function of general practice in the next ten or fifteen years, which happens to be the period of planning the hospital service. The basis of hospital planning is that outside the hospital service the practitioner and the local authority will be fulfilling their role according to the best of present standards. The future of general practice was bound up with the future of the hospital service; and he had been glad to announce the Government's acceptance of the Platt report, which suggested one way of broadening out the practitioner's work in association with the hospital service. If there had been a time when the general practitioner felt that the world had passed him by, that time had now decisively

gone. Throughout the National Health Service, people were eager to give him scope and importance. The danger rather lay in unthinking acceptance. But the college was ever seeking to replace platitude by precision, and only nine years after its formation it spoke with authority and had earned respect.

Dr. G. F. Abercrombie, the president, recapitulated Mr. Powell's past, outlined his present ("breakfast with Dr. Godber; elevenses with the Nurses; lunch with the Royal Society of Health from 12 till 4"), and promised to watch his future with interest, sympathy, and admiration; and Dr. K. M. Foster asked the Minister to give his office "such a length of stay as will please you and please the medical profession".

Lord Cohen of Birkenhead recalled that in 1950, even before the college's foundation, the Cohen Committee on postgraduate training had emphasised the association between practitioner and hospital; but those who forget history must relive it. The role of the practitioner was known: there *must* be somebody having continuous personal care of the patient, and he could not be replaced by congeries of specialists. The college's new motto, *cum scientia caritas*, embodied the whole truth of medicine as the general practitioner practises it in an advancing stage of technology.

Speaking at the request of the president, Sir Harry Guy Dain, who received an ovation, said he hoped that the Minister, as one who cared about the National Health Service, would continue to have it in his care until it evolved into a whole service instead of three parts. Having had a great deal to do with the Dawson report of 1920, he could not help thinking how appropriate some of the recommendations of that report would have been today if they had been adopted.

Central Middlesex Hospital, London

A new cardiothoracic department at this hospital was opened by Sir Harry Jephcott, chairman of Glaxo Laboratories, on Nov. 24. The cost (over £10,000) has been contributed by several industrial firms, and by patients and friends of the hospital. A further £2000 is still required for equipment.

The department contains a laboratory for investigation of respiratory disease by physiological methods and for biochemical studies of heart-disease. There is also a large clinical room, a library, an X-ray room, and offices for the staff. The approach to the department is being converted into a dayroom for patients on the cardiothoracic wards. It is being furnished from the hospital's free monies.

Osler Club of London

A joint meeting of this Club with the Francis Bacon Society is to be held on Wednesday, Dec. 6, at 8 P.M. at Gray's Inn, W.C.1., when the speakers will be Commander Martin Pares, Sir Geoffrey Keynes, and Mr. A. Dickson Wright.

An advertisement on p. 56 invites applications for the full-time post of junior assistant editor of *The Lancet*.

On Wednesday, Dec. 6, at 5 P.M. at the Radcliffe Infirmary, Oxford, the Medical Consilium will commemorate the bicentenary of the publication of J. B. Morgagni's *De Sedibus Morborum*.

A meeting of the Medical Association for the Prevention of War will be held on Thursday, Dec. 7, at 6.30 P.M., at Friends House, Euston Road, London, N.W.1, when Mr. Henry Usborne will speak on a Federation of Nations.

A meeting of the Sheffield Regional Psychiatric Association is to be held on Saturday, Dec. 9, at 11 A.M., at Whiteley Wood Clinic, Sheffield, when Prof. Desmond Curran will speak on the defence of amnesia in the criminal court.

The Hospitals Symphony Orchestra and the London Medical Orchestra will give a concert for the Marie Curie Foundation at the Central Hall, Westminster, London, S.W.1, on Thursday, Dec. 14, at 8 P.M. Tickets may be had from the secretary of the foundation, 124, Sloane Street, S.W.1.

The British Commonwealth Medical Graduates Society of New York has been started, and informal meetings will be held four times a year. It plans to provide an information service for colleagues in other parts of the Commonwealth. Further particulars may be had from the secretary, Dr. Mary Macfarlane, department of anæsthesia, The Presbyterian Hospital in the City of New York, 622, West 168th Street, New York, 32.

Diary of the Week

DEC. 3 TO 9

Sunday, 3rd

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, W.C.1
10.15 A.M. Mr. Wallace Black: Common Ear, Nose, and Throat Conditions.

Monday, 4th

POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road, W.12
4 P.M. Dr. H. E. Huxley: Mechanism of Muscular Contraction.
ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW, 242, St. Vincent Street, Glasgow
5.15 P.M. Prof. A. W. Kay: Management of Obscure Alimentary Bleeding. (Blackham lecture.)

Tuesday, 5th

ROYAL COLLEGE OF PHYSICIANS OF LONDON, Pall Mall East, S.W.1
8.30 P.M. Dr. K. D. Keele: Impact of Science on Clinical Methods. (Third FitzPatrick lecture.)
BRITISH POSTGRADUATE MEDICAL FEDERATION
5.30 P.M. (London School of Hygiene and Tropical Medicine, Keppel Street, W.C.1.) Dr. B. T. Donovan: Timing of Puberty.
ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1
5.30 P.M. *Pathology.* Dr. N. M. Hancox, Mr. S. J. Holt, Dr. A. J. Hale: Histochemistry and Cytochemistry.
ST. MARY'S HOSPITAL MEDICAL SCHOOL, W.2
5 P.M. Mr. Dennis Davey: Prediabetes and Pregnancy.
WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY, 91, Dean Street, W.1
5.30 P.M. Mr. I. R. McCaul: Surgery of Parkinsonism.
MANCHESTER MEDICAL SOCIETY
5 P.M. (Clinical Sciences Building, York Place, Manchester.) *Surgery.* Prof. L. N. Pyrah: Aspects of Renal Calculi.

Wednesday, 6th

POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road, W.12
2 P.M. Dr. K. Fotherby: Use of Steroid Hormone Investigations in the Diagnosis of Disease. (Second of two lectures.)
ROYAL SOCIETY OF MEDICINE
5.15 P.M. *History of Medicine.* Dr. F. N. L. Poynter: Southwood-Smith.
8 P.M. *Surgery.* Prof. A. G. R. Lowden, Mr. W. M. Capper, Mr. Rodney Maingot, Mr. Andrew Desmond: Abdominal Fistulæ.
INSTITUTE OF BIOLOGY
5.15 P.M. (Natural History Museum, Cromwell Road, S.W.7.) Dr. J. M. Tanner: Human Growth in its Comparative and Evolutionary Aspects. (Darwin lecture.)
INSTITUTE OF DERMATOLOGY, Lisle Street, W.C.2
5.30 P.M. Dr. K. V. Sanderson: Histology—Cellular Nævi and Melanomas.
INSTITUTE OF DISEASES OF THE CHEST, Brompton, S.W.3
5 P.M. Mr. J. R. Belcher: Mitral Incompetence.
MANCHESTER MEDICAL SOCIETY
4.30 P.M. (Medical School, University of Manchester.) *Medicine.* Dr. G. M. Komrower: Management of Congenital Adrenal Hyperplasia.
MEDICO-CHIRURGICAL SOCIETY OF EDINBURGH
8.30 P.M. (Royal College of Surgeons of Edinburgh, 18, Nicolson Street, Edinburgh.) Mr. N. W. Graham, Dr. J. W. Affleck: Implications of the Mental Health (Scotland) Act.

Thursday, 7th

ROYAL COLLEGE OF PHYSICIANS OF LONDON
8.30 P.M. Dr. Keele: Vision in Clinical Medicine. (Fourth FitzPatrick lecture.)
ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, W.C.2
5 P.M. Mr. J. B. M. Roberts: Spina Bifida and the Urinary Tract (Hunterian lecture.)
BRITISH POSTGRADUATE MEDICAL FEDERATION
5.30 P.M. (London School of Hygiene and Tropical Medicine.) Dr. F. Kingsley Sanders: Infective Nucleic Acids and Virus Synthesis.
ROYAL SOCIETY OF MEDICINE
8 P.M. *Neurology.* Dr. Macdonald Critchley, Dr. Edwin Bickerstaff, Dr. Raymond Greene, Mr. Geoffrey Knight: Migraine.
NUFFIELD ORTHOPÆDIC CENTRE, Wingfield-Morris Orthopædic Hospital, Oxford
8.30 P.M. Mr. Dillwyn Evans: Relapsed Club Foot.
LIVERPOOL MEDICAL INSTITUTION, 114, Mount Pleasant, Liverpool, 3
8 P.M. (Joint meeting with the Liverpool Psychiatric Club.) Dr. J. S. Madden, Dr. W. H. R. Cook, Dr. W. L. Selkirk: Alcoholism.
HONYMAN GILLESPIE LECTURE
5 P.M. (University New Buildings, Teviot Place, Edinburgh.) Dr. John Richmond: Observations on Hæmolytic Disease.

Friday, 8th

POSTGRADUATE MEDICAL SCHOOL OF LONDON
10 A.M. Mr. Walpole Lewin: Treatment of Head Injuries.
4 P.M. Prof. C. H. Stuart-Harris: Respiratory Virus Diseases.
PLYMOUTH MEDICAL SOCIETY
8.30 P.M. (North Friary House, Greenbank Terrace, Plymouth.) Prof. C. D. Calnan: New Forms of Contact Dermatitis.

Appointments

BALL, M. J., M.B., B.SC. Lond.: assistant M.O., Surrey.
CRAWFORD, LEONORA A., M.B. Lond., D.P.H., D.C.H.: senior assistant M.O., Middlesex (Southgate, Potters Bar, Wood Green, and Friern Barnet).
LLOYD-JAMES, T. A., M.B. Lond.: assistant M.O.H. and school M.O., Plymouth.
MARRABLE, I. H., M.R.C.S., D.T.M. & H.: assistant M.O., Surrey.
PALMER, J. R., M.B. Lond., D.P.M.: consultant psychiatrist, Reading area department of psychological medicine for duties at Fair Mile Hospital and Reading hospital group.
PETTIGREW, R. T., M.B. Glasg., F.F.A. R.C.S.: consultant anæsthetist, Edinburgh Northern hospital group.
RIDDOCH, MARGARET E., M.B. Edin., F.F.A. R.C.S., D.A.: consultant anæsthetist, Edinburgh Central hospital group.
SUTCLIFFE, MURIEL M. H., M.B. Sydney, B.SC. Manc., M.R.C.O.G.: maternal and child welfare M.O., Derbyshire.